April 16, 2002

SUBJECT: Atrazine: Response to Syngenta's Comments on the EPA's January 19, 2001 Revised Preliminary Human Health Risk Assessment and Associated Documents for the Reregistration Eligibility Decision (RED). PC Code: 080803. DP Barcode: D282042

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Please find attached the response document to Syngenta's Comments on the EPA's January 19, 2001, "Atrazine: HED's Revised Preliminary Human Health Risk Assessment (and Associated Documents) for the Reregistration Eligibility Decision (RED). HED responders included: Catherine Eiden, Linda Taylor, Gary Bangs, Dave Soderberg, and Jerry Blondell. Responders from EFED were Mary Frankenberry and Jim Lin. Responders from BEAD were Stephen Smearman.

Executive Summary

Syngenta provided an executive summary summarizing all of the specific comments contained in each of 10 attachments. Rather than responding to these summarized comments, HED, EFED, and BEAD responses to the specific comments contained in the individual attachments are provided in this document. Responses are organized by attachment. All comments expressed in the executive summary are covered under the responses to the individual attachments.

Response to Attachment 1 "Syngenta's Comments on EPA Revised Preliminary Risk Assessment Toxicology Chapter January 19, 2001.

Mammalian Toxicology

1. Toxicity Endpoint Selection: The chronic LH toxicological endpoint for atrazine should be determined using a benchmark dose approach derived from all of the appropriate data, including the Fischer-344 LH study. In the Preliminary Human Health Risk Assessment for Atrazine, EPA has incorrectly utilized NOAELs defined in studies characterizing the effects of atrazine on the endocrine system of rodents in the development of assessments estimating risk for infants, neonates, juveniles, and adults. In the preliminary assessment, the NOAEL from a 6-month chronic rodent study conducted in sexually mature female Sprague-Dawley rats was used to represent the intermediate-term exposure of infants, children, young adults, and adults. Syngenta recommends this preliminary determination be reconsidered because there are shorter duration studies targeting selected age brackets that better represent these population subgroups.

HED Response: Although the endpoint selected [estrous cycle alterations and LH surge attenuation] for intermediate-term exposure of infants, children, young adults, and adults is derived from a 6-month study in adult rats, the endpoint is a reasonable surrogate for atrazine CNS-hypothalamic disruption in children. These biomarkers of atrazine's neuroendocrine mode of action (i.e., LH surge attenuation and estrous cycle disruption) are considered to be applicable to the general population including infants and children given that they result from atrazine's CNS mode of action. It should be pointed out that the population of concern includes teenage children, and some functional portions of the CNS, such as the hypothalamic controls of reproductive cycling, are not mature until the second decade [Developmental Toxicology, 2nd ed., edited by c. A. Kimmel and J. Buelke-Sam, Raven Press, Ltd. NY (1994)]. Additionally, since this dose is the lowest NOAEL available in the toxicology database, it would be protective of other adverse effects, including those occurring in males, infants, and children. Therefore, given the uncertainty of atrazine's potential effect during development *via* the mode of toxicity of atrazine, the use of the NOAEL from the 6-month study is considered protective of the population of concern [infants and children]. *With respect to the issue of benchmark dose, see below.*

2. Selection of a Representative Species in a Probabilistic Evaluation: The approach traditionally selected by EPA of selecting an upper bound; i.e., conservative, estimate of exposure and using the most sensitive toxicological endpoint found in the most sensitive species evaluated is not

appropriate when a higher tier probabilistic assessment of exposure and risk is being conducted. In the case of atrazine, the toxicological mode-of-action data confirm that the Sprague-Dawley rat is not relevant to humans and the Fischer-344 rat is a more appropriate model. Additionally, the chronic LH toxicological endpoint for atrazine should be determined using a benchmark dose approach [NOEL, LED_{10}] derived from all three 6-month atrazine studies on LH, including the Fischer-344 LH study.

HED Response: Atrazine's effect on ovarian cycling, the pre-ovulatory LH surge, pregnancy, puberty, and suckling induced prolactin release are viewed as neuroendocrinopathies or biomarkers indicative of atrazine's ability to alter hypothalamic-pituitary function, and these biomarkers are considered to be applicable to the general population including infants and children given that they result from atrazine's central nervous system [CNS] mode of action. Additionally, it should be noted that atrazine's neuroendocrine effects have been demonstrated in several strains of rats [Sprague-Dawley, Long Evans, and Wistar]. Further, depending on the endpoint monitored, other strains of rat have demonstrated adverse effects following atrazine exposure at lower dose levels than in the SD strain [*e.g.*, pre- and post-implantation losses were observed in Holtzmann and Fischer 344 rats but not SD at comparable dose levels; 1-and 3-day exposures to atrazine suppressed LH and prolactin surges in Long-Evans but not SD rats]. The HED Cancer Assessment Review Committee [CARC] concluded that although atrazine exposure is not associated with apparent cancer consequences in humans, a potential for noncancer effects due to its ability to disrupt hypothalamic-pituitary function cannot be discounted.

Given the fact that disruption of the hypothalamic-pituitary-gonadal axis is applicable to all species, using the most sensitive species and endpoint is protective and consistent with EPA's traditional approach.

The Agency and OPP are still gaining experience with the BMD approach in general and continue to support this area of method development in risk assessment. Any model used and applied must be evaluated and reviewed carefully. Because the NOAEL and LOAEL (i.e, NOAEL was 1.8 mg/kg/day with a minimal response at 3.65 mg/kg/day) are close in the 6 month LH study, the NOAEL is considered appropriate to use at this time. However, the Agency will continue to explore appropriate dose response models for hormonal changes.

3. EPA's use of the FQPA Safety Factor for children: EPA's preliminary decision to retain the FQPA 10x safety factor is not supported by the data for all age groups and exposure durations and is an error.

HED Response: The determination that the FQPA SF is appropriate for all age groups is supported by the nature of the effect of concern [neuroendocrine disruption] and uncertainties with respect to possible effects from exposure throughout development, which have not been thoroughly examined. As stated in the SAP report, a potential for noncancer effects due to its ability to disrupt hypothalamic-pituitary function cannot be discounted. Hypothalamic GnRH controls pituitary hormone secretion (*e.g.,* LH, prolactin) in both humans and rats. The hypothalamic-pituitary axis is involved in the development of the reproductive system, and its

maintenance and functioning in adulthood. Additionally, reproductive hormones modulate the function of numerous other metabolic processes, including bone formation, and immune, CNS, and cardiovascular functions. Therefore, altered hypothalamic-pituitary function, which can potentially broadly affect an individual's functional status, is considered relevant to humans of all population subgroups. *See additional comments under Use of Additional 10X Safety Factor, below.*

With regard to increased quantitative susceptibility of the young in the preliminary assessment, a re-examination of the maternal body-weight gain data from the DACT rat developmental toxicity study indicates that there was a decrease in body-weight gain in the dams at 25 mg/kg/day [DACT] during the first 3 days of dosing [gestation days 6-8], and the magnitude of the decrease [32%] is considered to be evidence of maternal toxicity. Therefore, developmental toxicity and maternal toxicity occurred at the same dose level [25 mg/kg/day], and there is no apparent increased quantitative susceptibility following DACT exposure in this study. *See additional comments under DACT Developmental Toxicity, below.*

With regard to the completeness and reliability of the toxicology database, HED agrees with the registrant that all of the testing requirements [CFR 158.340] for food use of atrazine have been met, and the database is considered complete. However, as discussed below under *Use of Additional 10X Safety Factor,* hazard-based residual uncertainty remains.

The listing of General Population (including infants and children) in Table 8.2 Summary of the Toxicological Dose and Endpoints for Atrazine Use in Risk Assessment in the previous Toxicology Chapter of the RED for the acute dietary exposure risk assessment was in error. The population of concern for the acute dietary risk assessment is **Females between the ages of 13 and 50.** No appropriate endpoint attributable to a single exposure was identified for the General Population (including infants and children). This has been corrected [see Fourth Report of the HIARC on Atrazine/DACT; TXR NO. 0050592].

As described in the OPP guidance document entitled, "DETERMINATION OF THE APPROPRIATE FQPA SAFETY FACTOR(S) IN TOLERANCE ASSESSMENT", the approach used in determining the FQPA safety factor is a "weight-of-the-evidence" approach wherein all pertinent data, both hazard and exposure, are considered together for the pesticide under evaluation. The FQPA safety factor determination is informed by the risk characterization which includes an evaluation of the level of confidence in the hazard and exposure assessments and whether or not there are residual uncertainties identified. The FQPA safety factor determination is based on the way in which the risk assessment process handled completeness of the toxicology and exposure databases and potential for pre and postnatal toxicity as mandated by the FQPA. *See additional comments under Use of an Additional 10X Safety Factor below.*

4. Infant and Children Sensitivity Based on the fact that the lowest NOAEL for atrazine is derived from a chronic study where atrazine was administered to <u>adult</u> female rats for 6 months and studies evaluating developmental parameters display higher NOAELs than found in the adult animals indicates to the registrant that the developing organism is less sensitive than the adult.

HED Response: The registrant is correct in noting that the lowest atrazine NOAEL is derived from a chronic [6-month] rat toxicity study in adults. The other studies cited by the registrant reflect dosing for shorter periods of time. In general, higher doses of a compound over a short-time interval are required to elicit an effect, which can also be elicited at a lower dose level with continued exposure. The fact that the studies in which the young were dosed suggest that a higher dose is required to elicit an effect does not signify that the young are less sensitive. In most cases, dose selection may have resulted in the apparent difference. For example, in the 1996 Morseth [6 month] study cited in Table 1 [page 13] of the response, 3.65 is listed as the NOAEL and 29 is listed as the LOAEL. Comparing this to the postnatal day [PND] 1-4 study in which the doses shown in Figure 1 [page 12] are NOAEL 13 and LOAEL 25, the LOAELs are comparable [25 *vs*29], and a NOAEL of 3.65 would have been observed in the PND 1-4 study if it had been the dose tested. Comparing the 30-day studies between the young and adult, delayed vaginal opening was observed at 50 mg/kg/day in the young female rat and LH surge decrease was observed at 40 mg/kg/day in the adult. The dose spread [NOAEL-LOAEL] in the young rat study was 25-50 and the dose spread in the adult study was 5-40. Additionally, the parameter monitored in the adult studies [effect on the LH surge] was not monitored in the studies on the young.

Different endpoints can be affected at different dose levels and at different times following dosing, and the pre-ovulatory LH surge appears to be the most sensitive biomarker. Due to the lack of LH data for the young animal, the findings in the 6-month study are appropriate, and other data [1-day, 3-day, 21-day and 1-month studies] provide evidence that an effect on the LH surge can occur following exposure of any duration. Although it is recognized that the effects in the shorter duration studies were observed at higher dose levels, there is concern of the potential neuroendocrine effects of repeated atrazine exposure throughout all critical developmental periods, which have not been adequately characterized in the young animal. NOTE: The NOAEL selected for the 6-month study is based on a weight-of-evidence determination; i.e., LH surge attenuation and estrous cycle effects data .

In the discussion of the pubertal studies, the registrant comments on preputial separation and refers to the Stoker, *et al.* (2000) paper, suggesting that preputial separation occurs normally between 40 and 50 days of age [average 43 days]. The 40-50 day range encompasses all strains. What is not discussed by the registrant is the fact that within each strain of rat there is a defined range of days during which this developmental landmark occurs. The historical control data from the performing laboratory [personnel communication] show a mean value of 41.56±0.48 [SEM] and a range of 40-43. Therefore, contrary to the registrant's statement that the concurrent control's preputial separation was earlier than usual, the concurrent control was within the testing laboratory's historical control range. With regard to the issue of dose response, the researcher stated that the study is run in several blocks; i.e., not all of the animals are dosed at the same time. Since the findings were reproducible in each block, the researcher considered the observed delays to be real. An explanation as to why there is an apparent non-linear dose-response is not clear [there may be competing mechanisms]. The NOAEL for preputial separation is considered to be 6.25 mg/kg/day.

5. DACT Developmental Toxicity: In the developmental toxicity study conducted in rat on diaminochlorotriazine[6] EPA concluded that the fetal and maternal NOELs in this study were 2.5 and 25 mg/kg/day, respectively, whereas the study director at the performing laboratory concluded that the fetal and maternal NOELS were both 2.5 mg/kg/day. Based on this difference in interpretation, EPA has requested that Syngenta conduct a multigeneration reproduction study on diaminochlorotriazine. Sygnenta agrees that an additional developmental toxicity study is needed to better characterize the dose-response relationship because of the discrepancy in interpretation of this study by EPA and the performing laboratory.

HED Response: This point is moot. A re-examination of the maternal body-weight data from the developmental toxicity study on DACT has been performed, and it was determined that maternal toxicity [decreased body-weight gain] was evident during the initial dosing period [gestation days 6-8] at 25 mg/kg/day. Therefore, the NOAEL for maternal toxicity has been changed to 2.5 mg/kg/day, and the LOAEL for maternal toxicity is 25 mg/kg/day. Additionally, this indicates that no apparent increase in susceptibility/sensitivity was demonstrated in this study, since developmental effects were seen in the presence of maternal toxicity. The developmental NOAEL was 2.5 mg/kg/day based on increase incidences of incompletely ossified parietals, interparietals and unossified hyoids at 25 mg/kg/day (LOAEL). Following a reevaluation of the data by the HIARC [March 19, 2002], it was determined that a 2-generation reproduction study on DACT is not required.

It was also determined at the March 19, 2002 HIARC meeting that, based on structural similarities and the fact that the available data do not indicate that DACT would display any qualitative differences in factors of concern in regards to FQPA than seen with atrazine, the endpoints/dose levels selected for atrazine are applicable to DACT. Therefore, a separate HIARC assessment for DACT was not performed.

6. LH surge suppression studies: Syngenta has conducted two studies to directly compare the effects of atrazine and diaminochlorotriazine on LH surge suppression in the female Sprague-Dawley rat; EPA has reviewed the first study and the second study is expected to be submitted to EPA in March, 2001. The results indicate that the NOELs for atrazine and diaminochlorotriazine are approximately the same.

HED Response: HED has evaluated the registrant-sponsored LH data on DACT. It is to be noted that preliminary and unpublished studies from EPA's NHEERL [National Heath and Environmental Effects Research Laboratories (NHEERL) at Research Triangle Park, N.C. (Reproductive Toxicology Division) on delayed puberty in males also indicate that atrazine and DACT have similar NOAELs. Following an initial review of the new study [MRID 45471002], HED concluded that further analysis and review of these new data was needed before a definitive assessment could be conducted.

7. PBPK studies: Syngenta is developing a physiologically based pharmacokinetic model (PBPK) to characterize and scale tissue dose in rodent studies to tissue dose in primates. The model will then be adjusted for developing organisms, and the magnitude of the scale factors

will be determined. Using this method, Syngenta will determine the magnitude of the uncertainty factor needed when extrapolating from rodent to man.

HED Response: HED must await the submission of the referenced models and an assessment of the data/information and will consider such studies when made available by the Registrant.

8. Use of an Additional 10X Safety Factor: Syngenta stated that an additional 10X safety factor is not scientifically warranted based on available data and concluded that the available toxicology database for atrazine is sufficient to demonstrate with reasonable certainty that no harm will result to infants and young children from aggregate exposure to atrazine. All the evidence indicates that in fact developing organisms are less sensitive than are adults to atrazine.

HED Response: The toxicology data base for atrazine and DACT were re-evaluated by the HED Hazard Identification Assessment Review Committee (HIARC) on March 19, 2002. The HIARC concluded that there is no increased quantitative or qualitative susceptibility in any of the guideline studies conducted with atrazine in the rat, and there was no increased quantitative susceptibility in the atrazine rabbit prenatal developmental toxicity study. However, there is evidence of increased qualitative susceptibility in the rabbit study (increased resorptions at a dose level that resulted in decreased body-weight gain and clinical signs in the maternal animal).

There are other studies on atrazine that show evidence of endocrine disruption including a prostatitis study, a delayed puberty study in each sex, data on LH surge attenuation, and estrous cycle alterations. The primary underlying events that lead to mammary and pituitary tumor formation following atrazine exposure of Sprague-Dawley female rats involve disruption of the hypothalamic-pituitary-ovarian axis. Since aspects related to this axis are involved in reproductive and developmental competency, there is a concern for adverse reproductive and developmental effects in maternal animals and their offspring. Several special studies have been performed that show that treatment of pregnant rats with atrazine can lead to reproductive and developmental effects that may be associated with endocrine alterations. Additionally, the neurotoxicity seen in the non-guideline studies with atrazine is a central nervous system (CNS) toxicity - specifically, neurotransmitter and neuropeptide alterations at the level of the hypothalamus.

Studies in the open literature indicate increased qualitative susceptibility. Dosing of dams immediately following parturition [postnatal days 1-4] resulted in prostatitis in male offspring, and dosing of the young following weaning resulted in delayed puberty in both sexes. The mode of action for these two effects (prostate inflammation and delayed puberty) is believed to be similar to the mode of action described for atrazine-associated cancer and involves the CNS neuroendocrine alterations, specifically, neuroendocrine alterations at the hypothalamus.

Following a Degree of Concern Analysis [TXR No. 0050592], the HED Hazard Identification Assessment Review Committee [HIARC] concluded that an additional Special FQPA Safety Factor of 3X would be adequate to account for the **hazard-based** residual uncertainties for chronic dietary [cRfD] and residential (incidental oral, dermal, inhalation) exposures.

Additionally, it was concluded that an additional Special FQPA Safety Factor would not be required for acute dietary exposure [aRfD]. *Refer to the Risk Assessment on Atrazine for a discussion of the FQPA Safety Factor used for the various exposure scenarios [D272009].* The toxicology endpoints selected for risk assessment are all consistent with atrazine's mode of toxicity using the most sensitive endpoint with the lowest NOAEL (1.8 mg/kg/day). When comparing the effects observed in adults to those observed in the young, the HIARC considered the results of the pubertal assay. It is noted that delayed puberty was observed in both male and female offspring exposed to atrazine during the pubertal period (30 days for the males and 20 days for the females) and that clear NOAELs were established for this endpoint in both sexes (6.25 mg/kg/day in males; 12.5 mg/kg/day in females). If the lowest offspring NOAEL from this study is protected by a factor of 3X, the extrapolated NOAEL is 2 mg/kg/day. Comparing this value to the adult NOAEL of 1.8 mg/kg/day from the 6-month LH Surge study (used to establish the Chronic RfD and for the intermediate and chronic oral, dermal, and inhalation exposure scenarios) indicates that the young are not likely to be an order of magnitude more sensitive than the adult. Therefore, the HIARC concluded that a half-log reduction in the default Special FQPA Safety Factor is considered to be sufficiently protective of the concerns for this CNS mode of action in the young.

HIARC also recommended that the additional Special FQPA Safety Factor of 3X would not be required for Acute dietary exposures (aRfD) because the open literature data demonstrate that while the neuroendocrine effects caused by atrazine's mode of action could result from a single dose, this would only occur at very high doses (200-300 mg/kg), which is significantly higher than the 10 mg/kg level used to establish the Acute RfD. *Refer to the Risk Assessment on Atrazine for a discussion of the FQPA Safety Factor used for the various exposure scenarios.*

Taking into account the HIARC recommendation regarding residual concerns for uncertainties associated with Atrazine's neuroendocrine mode of action described above, the FQPA Safety Factor Committee (SFC) recommended that the default additional 10X FQPA Safety Factor be used in assessing dietary exposures because reliable data are not available to show a different factor would be safe; and that an additional 3X Special FQPA Safety Factor is adequate to protect the safety of infants and children in assessing residential exposure and risks. The rationale for that decision follows:

The Committee concluded that, as to dietary risk, the default 10X FQPA safety factor is statutorily required because of the absence of reliable evidence showing that an additional safety factor different than the statutory 10X default would be protective of infants and children. The principal grounds for this conclusion are:

1.) the HIARC identified residual concerns for the of effects of the neuroendocrine mode of action described for Atrazine on the development of the young (Refer to Section I.3.B.). These concerns could not be accounted for in the determination of toxicity endpoints and traditional uncertainty factors to be used in risk assessment; and

2.) residual concerns were also identified with regard to the drinking water exposure assessment.

The various water monitoring data sources which exist for Atrazine and its chlorinated metabolites indicate that exposure via drinking water sources is high in some of the systems that have been monitored and widespread low levels are commonly detected. Although it is known that there is significant, widespread exposure to Atrazine and its metabolites in drinking water, limitations in the extent, frequency, and compounds tested for in the monitoring data raise significant uncertainties regarding the level of exposure to Atrazine and its metabolites. Because of these uncertainties, the Committee concluded there is not reliable data to assign an additional safety factor that would adequately protect the safety of children by insuring that exposure in drinking water is not underestimated. The FQPA specifies that in the absence of such reliable data a default value of 10X is to be used as an additional safety factor for the protection of infants and children. As discussed below, the Committee believes there is reliable data to address the residual uncertainties regarding the neuroendocrine mode of action; however, because reliable data is not available as to all of the issues raising residual uncertainties, use of the default 10X factor is appropriate.

The Committee concluded that an additional Special FQPA safety factor of 3X is adequate for assessing residential exposures to Atrazine / DACT because the concerns for drinking water (described above) would have little or no impact on the residential exposure scenarios. The concerns for the effect of the neuroendocrine mode of action on the development of the young remain and the Committee concluded that there are reliable data to address these concerns through use of an additional Special FQPA Safety Factor of 3X (Refer to Section I.3.B for the rationale that this factor would be adequate to account for these hazard-based residual uncertainties).

Response to Attachment 2 "Syngenta's Comments on Use/Usage and Labeling Noted in the EPA's January 19, 2001 Atrazine: HED Revised Preliminary Human Health Risk Assessment (and associated documents) for the Reregistration Eligibility Decision (RED)".

Revised Preliminary Human Health Risk Assessment

1. Correction made as per registrant's comment.

2. The figure of 960 tons treated per day is based upon facility capacity, from various data sources, and therefore appropriate for use for this deterministic daily maximum exposure estimate and comparison to a short-term toxic dose. Syngenta's estimates are based on typical usage information, which is useful in characterizing the probability of mixing fertilizer with atrazine for eight hours per day. However, because the Agency is not assessing chronic handler exposure from treating fertilizer, a probabilistic analysis using average or typical quantities handled is not appropriate. Because the information provided is considered more specific to atrazine applications, it was used, *in toto*, to estimate a reasonable maximum commercial treatment rate of approximately 500 tons. Therefore both 500 tons and 960 tons per day were used in the revised assessment to provide a range of exposure estimates for risk management decisions.

3. Comment noted. Products registered to other registrants must necessarily be considered in the reregistration process.

Product and Residue Chemistry Chapters

1. The registrant has requested revocation of the *Perrenial rye grass* tolerance. HED will recommended for revocation of the 15 ppm tolerance for *Perrenial rye grass*. All product labels must be checked and the use cancelled. The registrant should request cancellation of the use.

In addition, the tolerance for *Grass, range* should be revoked and a crop group tolerance for Crop Group 17 (Grass, Forage, Fodder, and Hay) should be established under which range grasses would be covered. Residue data on representative grasses to support the crop group tolerance are recommended. This will include residue data on bermuda grass, bluegrass, and bromegrass or fescue from field trials conducted in concordance with the current label rates.

Occupational and Residential Exposure Assessment

1. References to atrazine use on sod and turf is more correctly noted a southern turfgrass. Comment noted.

2. Syngenta objects to terming some uses as "high rates". Syngenta notes that they only support a use rate of 2 lbs ai/A for CRP rangelands. They object to the terminology grasslands for those lands in the CRP restricted to OR, TX, OK, and NE. They also mention the restrictions on cutting and feeding grasses from these CRP lands, i.e., it is only allowed during drought conditions.

HED notes that there are labels (the 90DF formulations) that allow use rates up to 4 lbs. ai/A on southern turfgrass and rights-of-way. These rates are considered "high" relative to use rates of other atrazine products. As to use rates on CRP lands, registered rates are for up to 2.2 lbs product.

3. See response to comment 23 under response to Attachment 5. The Christmas tree worker exposure scenario is no longer warranted and will be removed from the assessment.

4. HED acknowledges Syngenta's note that they will submit information on dry fertilizer impregnation.

5. Syngenta comments that their SLN labels only allow application of atrazine to rights-of-way at 2 lbs ai/A. However, HED notes that there are labels with use rates as high as 4 lbs ai/A for use on rights-of-way, i.e., Oxon Italia 90DF (90% ai with rates up to 4.4 lbs product/acre). HED acknowledges these are not Syngenta products.

6. See response to comment 23 under response to Attachment 5. The Christmas tree worker exposure scenario is no longer warranted and will be removed from the assessment.

7. See response to comment 6 above.

Anticipated Residues and Acute and Chronic Dietary Exposure Assessments for Atrazine

1. Syngenta's comment infers that the percent crop treated (PCT) used in the dietary exposure and risk assessment, a 75% average and an 84% maximum for corn, is incorrect. They refer the to USDA NASS data for 1997 through 1999 as showing use at 70%. They used this value in their dietary assessments for corn and sorghum.

BEAD Response

BEAD believes the differences between Syngenta's estimates and OPP's estimates are because of the range of years used, and differences between the proprietary source data and USDA data used to establish the estimates. The original EPA estimate was based on the years 1990-1996. Syngenta states their estimate is based on data for the years 1997-1999 using the same USDA and proprietary sources EPA uses.

The Quantitative Usage Analysis (QUA) dated January 10, 2001 included PCT estimates for the period for 1990 to 1997; at that time the corn PCT estimates were revised to 75% crop treated for the weighted average, and 84% crop treated for the estimated maximum percent crop treated. Although EPA's most recent estimate for PCT for corn in 2000 is 68%, any updated PCT analysis would include data from a broader range of years than 2000. Although the estimate used in EPA's dietary assessment is slightly higher than the registrant's estimate of 70% crop treated for corn, the estimates risk from dietary exposures to atrazine is insignificant (< 1% of the acute and chronic populations adjusted doses or PADs). An update of the dietary assessments using the Syngenta PCT data would not result in any significant changes to the dietary assessments.

2. Syngenta comments that the sugarcane crop is treated at 70%, not 100% as assumed in OPP's dietary assessments.

BEAD Response

The estimated maximum percent crop treated for sugarcane was updated on January 10,2001. The revised estimate was changed from 100% crop treated to 95% crop treated. The EPA weighted average percent crop treated remains unchanged at 76% crop treated. This differs from Syngenta's estimate of 70% crop treated for sugarcane. However, the EPA estimate is supported by testimonials in the comments received from the Ohio Farm Bureau Federation (Comment #63, page 3, paragraph #7), "It is also applied to as much as 90 percent of U.S. sugarcane acreage."

3. Syngenta states that they do not support "woodlands" uses as categorized on the QUA.

BEAD Response

Labels exist that list both conservation reserve program and conifer sites. The survey used as the

basis of the QUA did not distinguish between uses on conifers versus woodlands.

4. Syngenta requested clarification of formulas and weighing factors used to arrive at PCT values.

BEAD Response

EPA/Office of Pesticide Programs (OPP) has made available to the public a document entitled "The Role of Use-Related Information in Pesticide Risk Assessment and Risk Management" on the internet at the following address: www.epa.gov/pesticides/use. The purpose of this paper is to provide an overview of the role of use-related information in the regulatory process in terms that can be understood by the public. Use-related data include information about how, where, when, why, and how much each pesticide is used in the U.S. This document was made available in August, 2000. The document details the rationale and methodology for the development of a Quantitative Usage Analysis (QUA) and supplies a sample of a QUA.

Section II details use-related information, the types of information, the extent of use, typical use practices, pesticide profile, how data are collected and analyzed and major sources of data. This type of information was considered to cumbersome to include in the QUA table but there are footnotes as to the sources of information and descriptions of lower bound values.

On pages 13-17, there is a detailed explanation of the methodology used to develop QUA's including how the weighted average and maximum percent crop treated estimates are derived.

The following is an excerpt from page 13 :

> "*The Automated Quantitative Usage Analysis (AQUA) program first standardizes data to generate consistent crop, product, and pesticide identifiers that often vary across different sources. For example, some sources name pesticides by their brand name and others name them by their active ingredient. Then, for agricultural pesticides, the program extracts state-level estimates of percent of crop treated, application rates, and number of applications from each source for each year (up to 10 years of data). Estimates from different sources are then averaged within each state, with weights used that reflect the size of the survey sample from a given source. Surveys with larger samples in the state are given greater weight since their data cover a larger proportion of actual use within that state. Estimates are then aggregated across states to generate national estimates (for each of several years) of quantitative use-related data. The estimates for the different years are then averaged using larger weights for more recent years, based on the observation that recent years are more representative of current normal use patterns than earlier years. The result is a national estimate of pesticide use for the following parameters:*
>
> *(a) number of U.S. acres grown*
> *(b) average number of acres treated (weights described above)*
> *(c) average percent of crop treated*
> *(d) average number of pounds of active ingredient (a.i.) applied*
> *(e) average annual application rate: pounds of a.i. applied per acre per year*
> *(f) average annual number of pesticide applications*

(g) average application rate: pounds of a.i. applied per acre per application

In addition to the estimates of weighted averages, the AQUA program also estimates the maximum likely number of acres treated, maximum percent of crop treated, and maximum total pounds of active ingredient. For these use parameters, rather than report the maximum observed level in the sample period, the AQUA estimates a probable (or likely) maximum. This is done because a particular maximum observed during the survey period may not represent conditions of the possible high pest infestation that would lead to the maximum likely pesticide use. Because the high end pest infestation may not have occurred during a survey period (even a 10 year period), more damaging infestations might occur resulting in higher levels of use than any observed levels."

EPA/OPP/BEAD welcomes further questions and inquiries concerning our methodology and data sources.

Response to Attachment 3 "Syngenta's Comments on EPA's January 18, 2001 Atrazine: HED Product and Residue Chemistry Chapters (Including the Tolerance Reassessment Summary) and Atrazine: Anticipated Residues and Acute and Chronic Dietary Exposure Assessments for Atrazine, Revised January 2001, and Related Information on Atrazine Residues in Corn and Sorghum in Attachment 7.

1. Any reference to BICEP has been removed as per comment.

2. "G27283 has been replaced with "G28273" as per comment.

3. The application rate for range grasses on CRP lands in NE, OR, OK, and TX under the 90 DF and 5L labels is 2.2 lbs product per acre.

4. There is no "#" sign on the pages noted. It is possible that the registrant's copy has been translated from WordPerfect to MS Word and therefore has some symbols reproduced incorrectly.

5. The line noted currently reads, "combined residues of ~ 0.1 ppm." It is possible that the registrant's copy has been translated from WordPerfect to MS Word and therefore has some symbols reproduced incorrectly.

6. Correction made as noted per comment.

7. See 4. above.

8. Correction made as noted in comment.

<u>Comments with Regard to Content and Conclusions of the Residue Chemistry Chapter</u>

1. Correction made as noted in comment.
2. Correction made as noted in comment.

3. Correction made as noted in comment.
4. Comment noted.

5. HED agrees that it is unproductive to treat sugarcane at concentrations that would result in phytotoxicity and is dropping the requirement for a study at 5X the seasonal application rate. HED does recommend another processing study using crops incurred with as large residues as possible from application of as much atrazine is safe, as late in the season as reasonable. If residue concentration is not seen, such a processing study might also demonstrate a significant decrease in residues in sugar cane sugar that would allow increased refinement in future atrazine exposure assessments.

6. HED will review the registrant's proposed study protocol for limited field trials for inadvertent residues in the Foliage of Legume Vegetables when it is submitted.

Comments with Regard to the Tolerance Reassessment Summary

Syngenta proposes lowering the tolerances for sweet and field corn forages to 1.5 ppm, and the tolerance for sorghum forage to 0.25 ppm. For post-emergent treatments the registrant proposes a change from a 30-day PHI to a 45-day PHI for sweet corn and sorghum forages, and from a 30-day PHI to a 60-day PHI for field corn forage. Thus eliminating the 30-day PHI for post-emergent uses on sweet and field corn, and sorghum forages. For pre-emergent treatments on sorghum, they propose a change from a 45-day PHI to a 60-day PHI. Pre-emergent treatments on sweet and field corn will retain the existing 45-day and 60-day PHI, respectively. Existing labels contain 21 and 30-day PHIs for corn and sorghum forages.

HED has reassessed the tolerance for sweet corn forages at 4.0 ppm based on field trial data showing the highest chlorotriazine residues detected at 3.2 ppm after a 1x treatment, and a 30-day PHI. Syngenta states that a sweet corn forage tolerance of 1.5 ppm is supported by data representing a 45-day PHI. Maximum chlorotriazine residues on sweet corn forage harvested 45 days after post-emergent treatments at the 1x rate expected to result in the highest residues (0.5 + 2.0 lbs ai/A) were approximately 1.15 ppm. HED concludes that once Syngenta amends all atrazine labels for post-emergent sweet corn use to allow a minimum PHI of 45 days, they can request the tolerance for sweet corn forage be lowered to 1.5 ppm.

HED has already reassessed the tolerance for field corn forage at 1.5 ppm based on the highest chlorotriazine residues detected at 1.1 ppm after a 1x treatment, at either a 30-day or a 60-day PHI. Maximum chlorotriazine residues on field corn forage after post-emergent treatments at the 1x rate (0.5 + 2.0 lbs ai/A) expected to result in the highest residues, which occurred in a sample harvested at a 60-day PHI, and were approximately 1.11 ppm. HED concludes that Syngenta should amend all atrazine labels for post-emergent field corn use to allow a minimum PHI of 60 days.

The tolerance for sorghum forage has already been reassessed at 0.5 ppm based on field trial data showing the highest chlorotriazine residues detected at 0.22 ppm after a 1x treatment, and a 23-

day PHI. Syngenta states that a sorghum forage tolerance of 0.25 ppm is supported by data representing a 45-day PHI. Maximum chlorotriazine residues on sorghum forage harvested 30 and 45 days after **post-emergent** treatments at the 1x rate were approximately 0.35 ppm and 0.09 ppm, respectively. Maximum chlorotriazine residues on sorghum forage harvested 45 and 60 days after **pre-emergent** treatments at the 1x rate were approximately 0.12 and 0.16 ppm, respectively. HED concludes that if Syngenta amends all atrazine labels for post-emergent sorghum use to allow a minimum PHI of 45 days, and for pre-emergent sorghum use to allow a minimum PHI of 60 days, they can request the tolerance for sorghum forage be lowered to 0.25 ppm.

Reassessed milk tolerance:

Syngenta proposes that lowering the sweet corn forage tolerance will lower the reassessed milk tolerance as the milk tolerance relates directly to the sweet corn forage tolerance used in estimating a maximum theoretical dietary burden for chlorotriazines in feeds fed to dairy cattle. HED has recalculated the maximum theoretical dietary burden (MTDB) for dairy cattle based on a reassessed sweet corn forage tolerance of 1.5 ppm. The resulting MTDB for dairy cattle is approximately 2.0 ppm chlorotriazines. Extrapolating the results from cattle feeding studies to this MTDB results in a reassessed milk tolerance of 0.03 ppm. Once Syngenta agrees to amend all atrazine labels to the proposed PHIs discussed above for sweet and field corn forage, and sorghum forage, they can propose lowering the milk tolerance based on available feeding studies and residue data.

Comments with Regard to Content and Conclusions of the Exposure Assessments

Syngenta submitted a revised chronic dietary assessment. In it they included small changes in % crop-treated data, and the ratio of pre- to post-emergent use. HED has reviewed Syngenta's assessment for dietary exposure to chlorotriazines and determined that the registrant's assessment does result in small incremental reductions in exposure; however, those reductions do not change the outcome of the overall aggregate exposure assessment for atrazine. Syngenta's dietary assessment results are compared to EPA's 2001 revised dietary assessment results in table 1.

Table 1. Chronic Dietary Exposure to Atrazine (mg/kg/day)

Population Subgroup	Syngenta Assessment	EPA 20001 Assessment	Risk Estimates (%PAD)
US population	0.000003	0.000005	<1%
Infants (< 1 year old)	0.000006	0.000008	<1%
Children (1 - 6 years old)	0.000010	0.000017	<1%

HED reports its risk estimates based on chronic dietary exposures as a percentage of a population adjusted dose (%PAD) for intermediate-term and chronic effects. Using either Syngenta's or EPA's 2001 results, the risk estimates for dietary exposure to chlorotriazine residues are reported

as < 1% PAD for intermediate-term and chronic effects.

Under HED's methodology for estimating aggregate exposures to chlorotriazines in food and drinking water, the drinking water exposure pathway is shown to be the dominant exposure pathway, and food exposures are shown to be insignificant by comparison. HED has taken the results of Syngenta's dietary assessment and used them to calculate the DWLOCs for infants for intermediate-term and chronic effects. The intermediate-term DWLOC for infants (< 1 year old) was calculated to be 12.55 ppb. Using EPA's 2001 dietary assessment the intermediate-term DWLOC for infants was calculated to be 12.54 ppb. The incremental change in the registrant's dietary exposure assessment translates to an insignificant effect on aggregate exposure to chlorotriazines in food and drinking water. HED does not anticipate further refinements to the dietary exposure assessments for the chlorotriazines as they are not expected to result in significant changes to the overall aggregate exposure assessment for the chlorotriazines.

Regarding the inclusion of wheat in the dietary assessment, PDP data from 1995 to 1997 showed 1563 samples of wheat analyzed, and 27 samples with detectable residues of atrazine (parent) ranging from 0.003 to 0.031 ppm. This appears to contradict the registrant's statement that residues of atrazine (parent) are not anticipated in wheat.

Hydroxy-triazine Residues in Livestock Feed Commodities

Syngenta argues that since the Agency has determined that there is no reasonable expectation of finite residues of hydroxy triazines in animal commodities, there is no need for tolerances or an enforcement method for hydroxy triazines in animal feed commodities, i.e., corn and sorghum forage, fodder and silage, and wheat forage, hay and straw. Because of the 180.6(a)3 classification for animal commodities, these commodities are excluded from any dietary assessment for the hydroxy triazines. However, tolerances for animal feed commodities are required for the purposes of detecting illegal or misuses of atrazine products on the commodities from which animal feedstuffs come. Therefore, tolerances as cited in the HED Product & Residue Chemistry Chapter (January 2001) are required. The previously submitted analytical method (AG-596) is suitable for enforcement purposes regarding hydroxy triazine compounds in plant commodities.

Hydroxy-triazine Residues in Direct Human Consumption Commodities

Syngenta argues that since method AG-596 determines GS-17794 (2-amino- 4-hydroxy-6-isopropylamino-s-triazine) and GS-17794 is the predominant hydroxy triazine detected in plant commodities consumed by humans, this compound can serve as a marker compound for all 4 hydroxy triazine compounds. In plant metabolism studies for corn, sorghum, and sugarcane, GS-17794 was the predominant hydroxy triazine metabolite accounting for 50 to 90% of the hydroxy triazines detected. On average GS-17794 accounts for 70% of the free hydroxy triazine compounds detected in forages, fodders, and sugarcane, and 50 to 70% of the free hydroxy triazine compounds detected in grains.

HED concludes that GS-17794 is a suitable marker compound for the hydroxy triazines and may be used to estimate total free hydroxy triazines in crops through the following formula:

X (ppm) GS-17794 ÷ 0.70 = total free hydroxy triazines (ppm).

Method AG-596 will be forwarded to ACB for PMV testing. An additional analytical method capable of determining all four of the hydroxy triazines is not warranted.

Response to Attachment 4 "Syngenta's Comments on EPA's January 19, 2001 Atrazine: HED's Revised Preliminary Human Health Risk Assessment for the Reregistration Eligibility Decision (RED)" Total Chloro-Triazine Concentrations in Surface Water Calculated from Atrazine Concentrations listed in the PLEX, VMS, and ARP Databases.

In general HED notes that most of the comments in Attachment 4 relate to the methodology used to estimate total chlorotriazine concentrations in surface water as annual or seasonal means. The methodology used by the OPP differs from that proposed and used by Syngenta. While HED relies on EFED to argue the merits of their approach, HED believes the point is not who estimated the "correct" value, because the exact value cannot be known with certainty unless daily samples were taken during the period for which an average was estimated. Although there are differences in the annual and seasonal averages estimated by the EFED and Syngenta, the differences are on the order of a few ppb for most CWS, or at most 2X for a few CWS, as seen in table 1 of Attachment 4 of Syngenta's comments. Both approaches are reasonable for a screening assessment. The end result of the methodology used by the Agency was to identify CWS under a deterministic screening assessment for inclusion in probabilistic assessments. The methodology preferred by Syngenta for estimating total annual and seasonal chlorotriazine concentrations has been used in these probabilistic assessments. Therefore, HED believes it is of little value to have EFED reanalyze total annual and seasonal chlorotriazine concentrations using Syngenta's methodology. Given the uncertainty surrounding any estimate of annual or seasonal average concentration values, HED has edited the drinking water exposure and risk assessment portion of the revised preliminary risk assessment to clarify that under the deterministic approach and methodologies used, seasonal or annual mean concentrations are estimates, and that any individual's exposure approaching, equal to, or above a level of concern is potential. A more refined estimate of exposures based on probabilistic assessments will be included in the final risk assessment.

<u>Methodology Corrections:</u>
Syngenta comments that seasonal and annual means should only be used to assess exposure for those time frames, i.e., 90 and 365 days, respectively, and that these means should not be used to establish exposure over longer time frames to assess chronic exposures. In several places in this attachment Syngenta also comments on the comparison of a 3-month (seasonal) average concentration to a DWLOC based on a chronic toxicological endpoint, and states that this is not scientifically appropriate.

HED agrees that seasonal (3-month) and annual means should not be used to establish long-term exposures over multi-year time frames. The seasonal means should be used to assess intermediate-term exposures, defined as 30 to 180 days, and the annual means may be used to assess annual exposures. Seasonal means can be used to assess seasonal exposures relevant to toxic effects (endpoints) that are believed to occur after intermediate-term exposure periods, i.e., exposure durations of 30 to 180 days. The endpoint based on the depression of the luteinizing hormone (LH) surge, taken from a 6 month (subchronic) study in the rat represents such a toxic effect. Depression of the LH surge was noted between 4 and 5 months of dosing in the 6-month study used to select the toxic endpoint for intermediate-term and chronic effects (HIARC memorandum dated 12/21/00). Time to the depression of the LH surge is dose dependent. The relevant effect is considered to represent both an intermediate-term and a chronic endpoint, and therefore, is appropriate for use in either an intermediate-term or a chronic risk assessment. This endpoint is particularly appropriate for assessing intermediate-term and chronic exposures to atrazine in drinking water, as these exposures occur both as seasonal pulses from weeks to months in duration, and chronically from months to years in duration, reflective of atrazine's use patterns and occurrence in drinking water. Basing seasonal exposure on seasonal means and comparing that exposure to the intermediate-term toxic endpoint is scientifically valid. Further, basing annual exposure on annual means and comparing that exposure to the chronic toxic endpoint (180 days to lifetime) is also scientifically valid. In this assessment, depression of the LH surge is both the intermediate-term and the chronic endpoint. Under the deterministic exposure and risk assessment, the DWLOCs for intermediate-term and chronic effects are the same value. Because the endpoint selected was not taken from a lifetime study, it is not used to assess lifetime exposures, and is not compared to exposure based on a multi-year or period mean concentration value for chlorotriazine residues in drinking water. For this reason, HED has not calculated multi-year or period means to use as the basis of lifetime exposure. Such an exposure assessment would have been appropriate if an assessment for a carcinogenic effect had been warranted. This will be clarified in the final revisions to the risk assessment.

Syngenta comments that the methodology used to estimate total chlorotriazine concentrations under the deterministic approach could be improved and made more robust by combining residue data for specific CWS across all the available data sets (VMS, ARP, and PLEX), and by estimating daily concentrations values (interpolating between actual measured data points) by assigning a residue value of a sample to each day going back one-half of the days to the previous sample date and forward one-half of the days to the next sampling date.

HED agrees with Syngenta that this methodology is more robust than the methodology used under the deterministic assessment, and has encouraged Syngenta to provide a probabilistic assessment for the CWS identified under the deterministic approach using their proposed methodology of combining data across data sets for specific CWS, and time-weighting residues as proposed rather than EFED reanalyzing all the data using the proposed methodology for time-weighting concentration measurements. Given the opportunity that Syngenta has to provide a more refined and robust probabilistic assessment using the preferred techniques of handling the monitoring data, there is little value in returning to the previous deterministic assessment at this stage. The preferred methodology should be used in the requested probabilistic assessment for

the previously identified CWS.

Syngenta comments that using their preferred methodology for time-weighting the monitoring data results in annual mean concentration values for chlorotriazines that exceed the intermediate-term to chronic DWLOC of 12.5 ppb in 5 CWS. This compares to HED's determination that 10 CWS had annual average chlorotriazine concentrations approaching, equal to, or greater than 12.5 ppb.

HED defers to the response above citing the requested probabilistic assessment, the results of which should provide a more refined assessment of exposures to chlorotriazines in drinking water in the CWS previously identified under HED's screening-level assessment. If the Agency's approach has erred on the side of conservatism under the deterministic screening assessment, the requested probabilistic assessment using Syngenta's preferred methodology of estimating time-weighted concentrations should provide the necessary refinements. HED notes that the exposure period of concern to the Agency for chlorotriazines in drinking water is the seasonal exposure occurring during the spring and summer months shortly after atrazine applications, and not the annual exposure.

Surface Water - Probabilistic Assessment:

Syngenta submitted a probabilistic assessment (Attachment 12) using their preferred method of estimating time-weighted averages for seasonal and annual concentrations of chlorotriazines for drinking water exposures for 28 CWS, 24 of which were identified for probabilistic assessment in HED's revised preliminary risk assessment. HED's review of that submission is contained in the memorandum (DP Barcode: 278468, C. Eiden, January xx, 2002). In that review, HED concludes:

1. At the 99.9th percentile of exposure, risk estimates for peak seasonal exposures of infants < 1 year old to chlorotriazine residues in drinking water exceed HED's level of concern, i.e., are greater than 100% of the PAD for intermediate-term and chronic effects, in 26 of the 28 CWS analyzed. Of these 26 CWS, 22 serve approximately 128,000 people. (The Shipman reservoir has been excluded as it is no longer serving as a source of drinking water). The population served by the remaining 3 CWS was unavailable. See Table 1.

2. At the 99th percentile of exposure, risk estimates for peak seasonal exposures of infants < 1 year old to chlorotriazine residues in drinking water exceed HED's level of concern in12 of the 28 CWS analyzed. Of these 12 CWS, 8 serve approximately 34,000 people. (The Shipman reservoir has been excluded as it is no longer serving as a source of drinking water). The population served by the remaining 3 CWS was unavailable. Risk estimates for 4 CWS equal 100% of the PAD for intermediate-term effects . See Table 2.

3. At the 95th percentile of exposure, risk estimates for peak seasonal exposures of infants < 1 year old to chlorotriazine residues in drinking water exceed HED's level of concern in 2 of the 28 CWS analyzed. Of these 2 CWS, 1 serves approximately 250 people, the other (Shipman reservoir) has been excluded as it is no longer serving as a source of drinking water. See Table 3.

[Note: The U.S. Census Bureau (2000) estimates that children under 1 year old represent 1.4% of the U.S. population.]

4. Risk estimates for children are less than 100% of the PAD (below HED's level of concern) for intermediate-term effects for all CWS analyzed at the 99th percentile of exposure. Risk estimates for adults are less than 100% of the PAD for intermediate-term effects for all CWS analyzed at the 99.9th percentile of exposure.

5. For the CWS assessed, the dominant exposure pathway for chlorotriazine residues is drinking water. Food exposures to chlorotriazines are insignificant (< 1% of the PAD for intermediate-term effects).

6. Exposure estimates are provided for specific age groups, but not for specific sexes. Exposures for male and female adults are combined.

7. A comparison of different models used to assess exposure to chlorotriazines in drinking water probabilistically indicated that if the same data sets are used and the same methodologies applied to the data, either model provides a similar distribution of exposures. However, if the same data sets are used but different methodologies are applied to the data, the resulting exposures will be different. The methodology used by Syngenta did not incorporate as much variability and randomness as the method preferred by OPP, and likely resulted in less refined estimates of exposure to chlorotriazines in drinking water.

Probabilistic exposure assessments for five of the 28 CWS were conducted using a methodology developed by Novigen, Inc. in consultation with OPP. The results of this assessment were compared to the results from Syngenta's assessment. Two of the 5 CWS assessed using the Novigen methodology resulted in risk estimates at the 99.9th percentile of exposure below HED's level of concern, while three had risk estimates above HED's level of concern. Using the Syngenta methodology, risk estimates for 4 of these 5 CWS were above HED's level of concern, and one was below.

Although the methodology used by Syngenta to assess exposure to chlorotriazine residues in drinking water probabilistically results in more refined estimates of exposure and risk for the 28 CWS assessed than the deterministic approach used in the revised preliminary risk assessment, depending on which percentile of exposure is selected as the basis of the risk estimate, the improvement in the risk estimates is limited to only a few CWS. The registrant may want to reconsider the methodology used in the submitted assessment. HED recommends the assessment for the 28 CWS be conducted using the methodology currently approved/used by OPP for cumulative dietary exposure assessment. This is OPP's preferred approach. Specifically, the exposure assessment should include: 1) rolling sequential 90-day exposure periods (90 consecutive days for a given year) across the entire 1993 to 2000 data set of chlorotriazine concentrations in finished drinking water for each CWS, 2) separate assessments for male and female adults, and 3) more recent consumption data from the USDA's Continuing Survey of Food Intake by Individuals (CSFII 1994 to 1996). The preferred methodology should allow sequential

daily chlorotriazine concentration values for rolling 90-day periods to be randomly matched with daily consumption values that also vary daily over the rolling 90-day periods for an individual as per CSFII records. This approach to the assessment maximizes randomness and variability, and should result in the most refined estimates of exposure using the available data.

Total Chloro-Triazine Concentrations in Surface Water Calculated from Atrazine Concentrations

1. Syngenta provides a comparison of the seasonal, and annual chlorotriazine concentrations as calculated by the EFED using arithmetic averages and by Syngenta using time-weighted concentrations for the CWS identified in HED's revised preliminary risk assessment. It can be seen through the comparison that the EFED's estimates of seasonal chlorotriazine concentrations are sometimes greater and sometimes less than the values estimated by Syngenta depending on the year and the database used. Overall, it looks as though EFED's estimates of seasonal chlorotriazine concentrations are somewhat higher than Syngenta's. This results in 9 CWS that may have been eliminated from the initial screen: West Salem, IL (1995), Flora, IL (1996), Sorento, IL (1996), Centralia, IL (1996), Wayne City, IL (1993), Batesville, IN (1997), N. Vernon, IN (1995), Bucklin, MO (1997), and Chariton, IA (1998). However, HED notes that for 6 of these CWS, Syngenta's estimated seasonal concentrations of chlorotriazines range from 9.95 to 11.25 ppb. These CWS have estimated seasonal chlorotriazine concentrations still approaching 12.5 ppb. Although Syngenta has made their point, HED's initial screening assessment was intended to be conservative and identify CWS for probabilistic assessment. All of the CWS identified in the Agency's revised preliminary risk assessment remain candidates for probabilistic assessments.

2. Syngenta comments on the method used by OPP to estimate annual mean concentrations of total chlorotriazines in CWS. Specifically, the registrant states that individual quarterly regression equations should have been applied to quarterly atrazine concentrations to estimate total chlorotriazines for each CWS, and then these values time-weighted within each quarter prior to averaging for an annual mean concentration of total chlorotriazines for each CWS.

Although combining the estimated means from individual quarters may have given slightly more precise estimates of the annual total than applying the regression equations to annual means, OPP did not judge the differences resulting from the two procedures as large enough to warrant rerunning the screening step in the assessment. Because EPA's regression equations gave slightly lower estimates overall than Syngenta's, the results showed some CWSs higher in the Syngenta response than in EPA's draft chapter, and some lower. In the end, the purpose of the first step was to serve as a method for screening CWSs to be selected for use in the probabilistic assessment, where results from more frequent monitoring would be used to better estimate total chlorotriazine levels for different periods of duration. In this initial stage, therefore, OPP took steps to summarize the overall levels and ultimately select systems for inclusion into a more refined characterization of risk.

3. Syngenta states that OPP should have used time-weighting in estimating the seasonal mean total chlorotriazine concentrations for CWS in the VMS and ARP databases.

On this comment, HED refers to the general comment at the beginning of this section of responses to comments in Attachment 4. Further, where sampling frequency remains the same within a season or quarter, as was the case for much of the VMS and ARP data, the time-weighted mean will be the same as the arithmetic mean for that quarter. Annual means employing data from these quarters may be calculated slightly differently. However, as stated above, this assessment produced general estimates of levels that were only a few parts per billion different between the two documents, and subsequent to which a more refined probabilistic assessment is being performed. Also, see response to comment #17 below.

4. Syngenta comments that seasonal mean concentrations estimated by EFED were not time-weighted, and that the seasonal means reported for six CWS in Illinois in 1993 were based on one sample in the VMS during June, and therefore, were not representative of actual seasonal (quarterly 3-month) mean concentrations across May , June, and July as stated by HED. They state that a 3-month mean from June through August would be more representative of a seasonal mean for these sic CWS in Illinois that were included in table 11 of the revised preliminary risk assessment.

HED concedes that the seasonal mean concentrations estimated by EFED were not time-weighted, but were estimated based on arithmetic averaging. HED defers to its general comment on this issue presented at the beginning of this section. HED also concedes the error in the risk assessment document regarding the six CWS in Illinois in 1993 included in table 11. The reported seasonal means for these six CWS ranged from a high of 61.61 ppb for the CWS at Salem, IL to 19.52 ppb for the CWS at Palmyra, IL. These values are based on one sample taken at the end of June at each of these CWS, and as such do not represent a seasonal mean values for chlorotriazines in the drinking water in 1993 at these CWS. Syngenta estimated 3-month means for these six CWS using data from June through August. The resulting seasonal time-weighted means as reported in table 2 of Attachment 4 of Syngenta's comments document are: 26.53 ppb (Salem, IL), 20.83 ppb (Farina, IL), 12.16 ppb (Kinmundy, IL), 19.48 ppb (Shipman, IL), 13.22 ppb (ADGPTV, IL), and 16.79 ppb (Palmyra, IL). HED will correct the notation for these CWS and clarify that the values reported in table 11 represent one sample in June and not a seasonal mean value for these CWS. HED will also add the Synenta estimates of seasonal means for June through August for these CWS to table 11. However, the six CWS will remain in table 11 identified as good candidates for inclusion in a probabilistic assessment as the 3-month average concentration is still approaching, equal to, or greater than 12.5 ppb.

The 3-month period, mid-April through mid-July, is the period most likely to have the highest seasonal mean concentrations of chlorotriazines in surface water. Atrazine use revolves around typical planting dates for corn, April 22 - May 28 in the Midwest (corn belt); most active between April 30 and May 18 (see table below). Most atrazine use on corn occurs pre/at planting, approximately 70% of total, with the remainder applied soon thereafter. Maximum seasonal concentrations should occur by end of June. Although the single samples collected in June 1993 under the VMS at each of the six CWS do not represent seasonal means, it is indicative of potentially high residues in the April-June period that were missed for 1993.

Method	Stage	Date(s)	Range	Most Active
Ground	Planting	May 9	Apr22-May28	Apr 30-May18
Ground	Planting	May 9	Apr22-May28	Apr 30-May18
Ground	Planting	May 9	Apr22-May28	Apr 30-May18
Ground	Planting	May 9	Apr22-May28	Apr 30-May18

5. Syngenta comments that 4 of the 10 CWS listed in the revised preliminary risk assessment as having annual average concentrations of concern should be deleted because they are less than 12. 5 ppb, the intermediate-term to chronic DWLOC. They also comment that their calculated values for annual average concentrations should replace those calculated by the EFED in table 13.

HED disagrees with Syngenta on these points. As stated in the revised preliminary risk assessment, CWS with total chlorotriazine concentrations approaching, equal to or greater than 12.5 ppb were identified under the screen for inclusion in a probabilistic assessment. The CWS previously identified remain candidates for probabilistic assessment. The estimated chlorotriazine annual average concentrations provided by Syngenta are slightly different from those estimated by the EFED and result in no changes to the CWS identified for probabilistic assessments. However, Syngenta's estimates of annual average concentrations of atrazine and the chlorinated metabolites will be included table 13 with EFED's estimates based on arithmetic averaging for comparison.

6. See responses to #1 and #5 above.

7. See response to comment # 4 above. Appropriate changes will be made to table 14 to note that the seasonal mean concentrations reported for the CWS in IL included for 1993 are based on one sample in June of 1993 taken at each of these CWS, and do not represent a seasonal (3-month) average concentration. Syngenta's estimates of time-weighted mean concentrations at these CWS have been included in table 14, as well. However these CWS will remain in table 14, identified as good candidates for inclusion in a probabilistic assessment.

8. See responses to #1 and #5 above.

9. Syngenta comments that EPA's comparison of a seasonal mean for chlorotriazines against the DWLOC of 12.5 ppb for intermediate-term and chronic effects is scientifically invalid. Instead, EPA should compare this DWLOC to period mean concentrations of chlorotriazines.

HED disagrees that seasonal (3-month) means should not be compared against the DWLOC of 12.5 ppb. The seasonal means should be used to assess intermediate-term exposures, defined as 30 to 180 days. Seasonal means can be used to assess seasonal exposures relevant to toxic effects (endpoints) that are believed to occur after intermediate-term exposure periods, i.e., exposure durations of 30 to 180 days. The endpoint based on the depression of the luteinizing hormone (LH) surge, taken from a 6 month (subchronic) study in the rat, represents such a toxic effect. Depression of the LH surge was noted between 4 and 5 months of dosing in the 6-month study

used to select the toxic endpoint for intermediate-term and chronic effects (HIARC memorandum dated 12/21/00). Time to the depression of the LH surge is dose dependent. The relevant effect is considered to represent both an intermediate-term and a chronic endpoint, and therefore, is appropriate for use in either an intermediate-term or a chronic risk assessment. This endpoint is particularly appropriate for assessing intermediate-term and chronic exposures to atrazine in drinking water, as these exposures occur both as seasonal pulses from weeks to months in duration, and chronically from months to years in duration, reflective of atrazine's use patterns and occurrence in drinking water. Basing seasonal exposure on seasonal means and comparing that exposure to the intermediate-term toxic endpoint is scientifically valid.

Further, basing annual exposure on annual means and comparing that exposure to the chronic toxic endpoint (180 days to lifetime) is also scientifically valid. An assessment spanning 180 days to 365 days falls within the chronic exposure duration. In this assessment, depression of the LH surge is both the intermediate-term and the chronic endpoint. HED selected the relevant endpoint as a biomarker of potential neuroendocrinopathies in humans. The effect in the rat occurs naturally at 9 months of age, and further testing beyond that point would be meaningless for this particular endpoint. For the effect of concern, seasonal exposures to atrazine are relevant. Under the deterministic exposure and risk assessment, the DWLOCs for intermediate-term and chronic effects are the same value. Because the endpoint selected was not taken from a lifetime study, it is not used to assess lifetime exposures, and is not compared to exposure based on a multi-year or period mean concentration value for chlorotriazine residues in drinking water. For this reason, HED has not calculated multi-year or period means to use as the basis of lifetime exposure. Such an exposure assessment would have been appropriate if an assessment for a carcinogenic effect had been warranted. This will be clarified in the final revisions to the risk assessment.

10. See response to #9.

11. See response to #9.

12. See response to #9.

13. See response to #9.

14. Comment noted. Typos will be corrected as per comment.

15. The figures in the appendices referenced have been removed.

16. The figures in the appendices referenced have been removed.

17. Syngenta provides a comparison of the seasonal, and annual chlorotriazine concentrations as calculated by the EFED using arithmetic averages and by Syngenta using time-weighted concentrations for the CWS identified in HED's revised preliminary risk assessment. It can be seen through the comparison that the EFED's estimates of seasonal chlorotriazine concentrations

are sometimes greater and sometimes less than the values estimated by Syngenta depending on the year and the database used. Overall, it looks as though EFED's estimates of seasonal chlorotriazine concentrations are somewhat higher than Syngenta's. This results in 9 CWS that may have been eliminated from the initial screen: West Salem, IL (1995), Flora, IL (1996), Sorento, IL (1996), Centralia, IL (1996), Wayne City, IL (1993), Batesville, IN (1997), N. Vernon, IN (1995), Bucklin, MO (1997), and Chariton, IA (1998). However, HED notes that for 6 of these CWS, Syngenta's estimated seasonal concentrations of chlorotriazines range from 9.95 to 11.25 ppb. These CWS have estimated seasonal chlorotriazine concentrations still approaching 12.5 ppb. Although Syngenta has made their point, HED's initial screening assessment was intended to be conservative and identify CWS for probabilistic assessment. As stated in the revised preliminary risk assessment, CWS with total chlorotriazine concentrations approaching, equal to or greater than 12.5 ppb were identified under the screen for inclusion in a probabilistic assessment. The CWS previously identified in the revised preliminary risk assessment remain candidates for probabilistic assessment.

18. HED disagrees with this comment. The CWS serving Palmyra-Modesto had chlorotriazine concentrations of 19.52 ppb (1993) and 21.92 ppb (1994) by EFED estimates, and 23.83 ppb and 16.79 ppb, respectively by Syngenta estimates. As stated previously, the purpose of the screen was to identify CWS with chlorotriazine concentrations approaching, equal to, or greater than calculated DWLOC values for inclusion in probabilistic assessments. In 1994 the CWS at Palmyra-Modesto was clearly approaching 18 ppb.

19. See response to #18.

20. See response to #18.

21. Corrected typo as per comment.

22. See response to #17.

23. See response to #17.

24. See response to #17.

25. See response to #17.

26. See response to #17.

27. See response to #17.

28. See response to #17.

29. All references to seasonal mean concentrations will be clarified to note that these are "estimates of seasonal mean concentrations". Line 10 on page 74 will be edited to read, ...

"Based on estimates of seasonal mean concentrations in 11 CWS, potentially 49,500 people may have been exposed to average seasonal concentrations approaching, equal to, or greater than 18 ppb....."

30. See response to #17.

31 through 33. [Ask EFED/Jim about this one.]

34 through 39. See response to #17.

40 through 44. See response to #17.

45. Corrected as per registrant's comment.

46. Could not find this typographic error.

47 through 49. Corrected as per registrant's comment.

50 through 52. Changed as per comment. See responses to #4 and #7 above.

53 through 54. Syngenta provides a comparison of the seasonal, and annual chlorotriazine concentrations as calculated by the EFED using arithmetic averages and by Syngenta using time-weighted concentrations for the CWS identified in HED's revised preliminary risk assessment. It can be seen through the comparison that the EFED's estimates of seasonal chlorotriazine concentrations are sometimes greater and sometimes lesser than the values estimated by Syngenta depending on the year and the database used. Overall, it looks as though EFED's estimates of seasonal chlorotriazine concentrations are somewhat higher than Syngenta's. This results in 9 CWS that may have been eliminated from the initial screen: West Salem, IL (1995), Flora, IL (1996), Sorento, IL (1996), Centralia, IL (1996), Wayne City, IL (1993), Batesville, IN (1997), N. Vernon, IN (1995), Bucklin, MO (1997), and Chariton, IA (1998). However, HED notes that for 6 of these CWS, Syngenta's estimated seasonal concentrations of chlorotriazines range from 9.95 to 11.25 ppb. These CWS have estimated seasonal chlorotriazine concentrations still approaching 12.5 ppb. Although Syngenta has made their point, HED's initial screening assessment was intended to be conservative and identify CWS for probabilistic assessment. As stated in the revised preliminary risk assessment, CWS with total chlorotriazine concentrations approaching, equal to or greater than 12.5 ppb were identified under the screen for inclusion in a probabilistic assessment. The CWS previously identified in the revised preliminary risk assessment remain candidates for probabilistic assessment.

55. Comment noted.

56 through 57. Changed as per comment.

58 through 59. Changed as noted per comment. See responses to #4 and #7 above.

60 through 63. See response to 53 through 54.

64. Changed as per comment.

65. Changed as per comment. See responses to #4 and #7 above.

66. See response to 53 through 54.

67. Changed as per comment.

68. Changed as per comment.

69. The PLEX database was used. Edited as noted.

70. HED acknowledges the comment and has confirmed the data presented by Syngenta on the CWS identified in Appendix E. In the preliminary assessment, HED identified 36 CWS with quarterly maximum concentrations above 18 ppb. In the 60-day public comments, Syngenta supplied seasonal mean concentrations for 18 of these CWS. Several of the CWS initially identified with quarterly maxima of concern were included in the VMS and ARP databases, and seasonal mean concentration values available for these CWS have been below levels of concern since 1995 or 1996. HED has removed these 18 CWS from the appendix, and notes that as they have been included in either the VMS, ARP, or both and are continuing to be monitored, no further action on these CWS are warranted. However, the remaining 18 CWS lack sufficient seasonal monitoring data to estimate the seasonal mean concentrations and the maximum quarterly concentration recorded in the PLEX database is still of concern for these 18 CWS. HED still considers these CWS as candidates for inclusion in the VMS monitoring program so weekly samples during the high-use season can be collected and used to estimate seasonal concentrations of total chlorotriazines.

In addition, HED has identified another 34 CWS in PLEX with quarterly maxima of 12.5 ppb or greater. HED considers these CWS as candidates for inclusion in the VMS monitoring program, as well, unless already included.

The table below contains 52 CWS for inclusion in the ongoing VMS program.

Community Water Systems (CWS) with Annual Maximum Concentrations of Atrazine plus Chloro-Metabolites Equal to or Greater than 12.5 ppb			
Year	CWS	Concentrations (ppb)	Comment
1998	Kansas City, KS	14.42	Self
1998	Defiance, OH	13.63	Self
1998	Ayersville, OH	13.63	Purchases from Defiance

Community Water Systems (CWS) with Annual Maximum Concentrations of Atrazine plus Chloro-Metabolites Equal to or Greater than 12.5 ppb			
Year	CWS	Concentrations (ppb)	Comment
1998	Cristi Meadows Subdivision, OH	13.63	Purchases from Defiance
1998	Brunersburg, OH	13.63	Purchases from Defiance
1998	Village of Blanchester, OH	12.47	Self
1998	Glasgow, MO	15.69	Self
1998	Howard Co. PWD #2	15.69	Purchase from Glasgow
1998	Waverly, IL		Self
1997	Newark, OH	29.7	Self
1997	Delaware, OH	19.8	Self
1997	Lake of the Woods	18.1	Self
1997	Napoleon, OH	17.9	Self
1997	Liberty Center, OH	17.9	Purchased water from Napoleon
1997	Florida City, OH	17.9	Purchased water from Napoleon
1997	Village of Malinta, OH	17.9	Purchased water from Napoleon
1997	Aquilla Water Supply District, TX	15.13	Self
1997	Brandon-Irene Water Supply Corp. TX	15.13	Self
1997	Chatt Water Supply Corp., TX	15.13	Self
1997	Files Valley Water Corp.	15.13	Self
1997	Hill Co. Water Corp., TX	15.13	Self
1997	Milford City, TX	15.13	Self
1997	City of Bynum, TX	15.13	Self
1997	Piqua, OH	14.31	Self
1997	Village of Mt. Orab, OH	12.87	Self
1997	Clermont Co., OH	12.62	Self
1996	Sardinia, OH	55.2	
1996	Louisville, IL	24.3	
1996	Osawatomie, KS	17.3	
1996	Miami Co. RWD #1, KS	17.3	Purchased water from Osawatomie
1996	Miami Co. RWD #3, KS	17.3	Purchased water from Osawatomie

Community Water Systems (CWS) with Annual Maximum Concentrations of Atrazine plus Chloro-Metabolites Equal to or Greater than 12.5 ppb			
Year	CWS	Concentrations (ppb)	Comment
1996	City of Osage, KS	15.84	Self
1996	Osage Co. RWD #7, KS	15.84	Purchased from City of Osage
1996	City of Reading	15.84	Purchased from City of Osage
1996	Osage Co. RWD # 6, KS	15.84	Purchased from City of Osage
1996	Omaha, IL	15.84	Self
1996	Village of Williamsburg, OH	14.56	Self
1996	City of Upper Sandusky, OH	14.38	Self
1996	Keysport, IL	14.42	Self
1994	Carthage, IL	15.84	Self
1994	Andersen Co., RWD #2, KS	15.84	Self
1994	Keysport, IL	18.7	Self
1994	Emma, MO	14.42	Self
1994	Louisville, IL	18.7	Self
1994	Vandali, IL	13.29	Self
1994	Canton	12.71	Self
1994	Cuba, IL	12.71	Purchases from Canton
1994	Norris, IL		Purchases from Canton
1994	Dunfer, IL		Purchases from Canton
1993	Three Rivers, IN*	20.1	
1993	New Haven, IN	20.1	Purchased water from Three Rivers
1993	Sunymede, IN	20.1	Purchased water from Three Rivers

The CWS serving Three Rivers, IN was not included in the VMS databases available to HED.

71 through 73. Comments missing or out of sequence.

74. See response to 50 through 52.

75. Changed as per comment. See responses to #4 and #6.

76. Because the endpoint selected was not taken from a lifetime study, it is not used to assess lifetime exposures, and is not compared to exposure based on a multi-year or period mean

concentration value for chlorotriazine residues in drinking water. For this reason, HED has not calculated multi-year or period means to use as the basis of lifetime exposure. Such an exposure assessment would have been appropriate if an assessment for a carcinogenic effect had been warranted. This will be clarified in the final revisions to the risk assessment.

Response to Attachment 5 "Syngenta's Comments on EPA's January 19, 2001 Atrazine: HED's Revised Preliminary Human Health Risk Assessment for the Reregistration Eligibility Decision (RED)" and the January 18, 2001 "Occupational and Residential Exposure Assessment and Recommendations for the Reregistration Eligibility Decision Document".

In response to the HED's Revised Preliminary Human Health Risk Assessment for atrazine, Syngenta provided the Agency with a cogent, well-organized document which included considerable supportive information. This memorandum considers the points taken as a whole, together with the documentation provided by Syngenta. Therefore the HED response will address each of the unique comments or issues raised and related comments at the same time.

Comments:

1. Page 6, 1st Paragraph, Line 7: The arbitrary aggregation of all potential activities that a person may do in an 8 hour period on a pesticide treated lawn (4 hrs of golf + mowing 2 hrs + 2 hrs of high-contact activity) immediately following an application is unrealistic. There are no data to form a basis for such a risk assessment nor is this type of risk manipulation sanctioned in the EPA Residential SOPs.

HED Response:
There is considerable uncertainty involved in predicting which activities may co-occur on treated lawns. However, the substantive point being made is that low-contact activities did not exceed the level of concern for adults, whereas the high-contact ("play") activities exceed the level of concern. The text will be changed to make this point without quantifying an aggregate dermal postapplication exposure. The dose from different exposure routes may reasonably be aggregated, as shown in the overall health risk assessment for atrazine.

2. Page 6, 2nd Paragraph: EPA mentions that there are several application methods that homeowners can use to apply atrazine to their yards; however, only the one method which results in a risk below the required MOE of 1000 is cited. To provide an unbiased summary, the other scenarios (spot treatment with hand pump and entire treatment with granular push spreader) should also be cited for comparison purposes.

HED Response:
The residential risk assessment has been revised using the ORETF data instead of the lower-confidence PHED data. Hand application methods have been removed from the assessment as the registrant has committed to labeling changes to prohibit hand application. The resulting assessment indicates that residential application methods do not result in exposures which exceed

the level of concern (i.e., all MOEs are greater than 1000).

3. Page 6, 3rd Paragraph: This wet/sticky hand scenario has not been adequately peer reviewed and should not be included in any assessment until properly evaluated and the data availability and needs are understood. There are no data to presume that results from a corn dislodgeable foliar residue study in any way represent transfer of pesticide residues from turf to a child's moist hand, so the corn DFR value should not be used to justify the 5% transfer factor. The default 5% transfer rate should in fact be replaced by the actual turf transferable residue data for atrazine adjusted for wet hands. As seen in the Clothier (2000) study, a 3-fold increase in wet versus dry hand transfer should be used until more relevant data are developed for this scenario in turf.

HED Response:

The corn DFR data have been replaced in the assessment by the use of standard residue of 5% of the total application rate to turf for transfer from wet or sticky hands. The transfer efficiency values are based on Exposure SAC Policy 12, *Recommended Revisions to the Standard Operating Procedures (SOPs) for Residential Exposure Assessments*, which were based on evidence presented at the Science Advisory Panel in December 2000, and address the transfer of pesticide residues to wet hands for use in non-dietary ingestion assessments. These are intended to provide a reasonable but high-end dermal exposure estimate when used with the revised transfer coefficients in Policy 12 for dermal exposure assessments. The document strongly urges assessors to use caution when using Occupational and Residential Exposure Task Force (ORETF) member Turf Transferable Residue (TTR) studies with the current transfer coefficients as this combination may under-predict dermal exposure. The ORETF has submitted a post application dermal exposure model for use with member TTR studies. This document is under review and will be presented to the Exposure SAC when all the issues are discussed and addressed by the ORETF.

The 5% transfer factor is based on data by Clothier (2000). Clothier measured percent transfer efficiency means of 0.156% (Std. Dev 0.138%), 2.72% (Std. Dev. 1.12%) 4.18% (Std Dev. 1.53%) for the pesticides chlorpyrifos, chlorothalonil, and cyfluthrin, respectively. The results are based on single hand presses of volunteers hands (wetted with their own saliva) onto St. Augustine turf treated with the above mentioned pesticides. These types of transfer efficiency data are needed to assess the hand-to-mouth exposure pathway when using hand-to-mouth frequency data based on videotapes or other observational data as discussed below under frequency. The wet values were 2 to 3 times higher than similar hand presses performed by volunteers whose hands were dry.

It should be noted that Syngenta has committed to conducting a dermal hand-press transfer study for granular atrazine product.

4. Page 6: 5th Paragraph: The label that permits professional application to "corn in the home garden" is an outdated label (accepted by EPA 4/18/89), which has been replaced by the label

(accepted 10/28/96) which does not allow this application scenario.

HED Response:
The newest label for Reg No 829-268 Atrazine 4L, accepted 10/28/96, no longer has the home corn use in question. This use will be removed from the revised risk assessment.

5. Page 7: 2nd Paragraph, Line 2: According to discussions on March 21, 2001, between the ORETF and representatives from EPA, it appears that the review of the ORETF mixer/loader/applicator monitoring data is complete and this data are viewed as high confidence. Therefore the statement "these data sets have not yet been fully compared, and therefore there are significant uncertainties in the risk estimates" is incorrect and should be removed.

HED Response:
The data review process was finalized in April, 2001, and the language in question will be updated in the revised risk assessment.

6. Page 7, 2nd Paragraph, Line 5: As this section relates to uncertainties in the risk assessments, it should be noted that there is a large amount of uncertainty in the oral ingestion scenarios and that these models are based on very conservative estimates of time and activity parameters that have not been validated.

HED Response:
There are substantial uncertainties in all of the exposure estimates involving human activity factors. However, the Recommended Revisions to the Residential SOPs (02/01) a.k.a. HED Exposure SAC Policy 12, include refinements of several of the activity factors. Overall, the revisions have resulted in more refined, less conservative SOPs. For example, the hand-to-mouth scenario now uses 3 fingers instead of the whole hand, a 50% saliva extraction factor instead of 100%, and the frequency selected (20 events/hour) is based on the 90th percentile of observed hand-mouth transfer frequency. Reed et al., (1999) reported hourly frequencies of hand-to-mouth events in pre school children aged 2 to 5 years based on observations using video tapes. The data consist of 20 children at daycare centers and 10 children at home. A range of 0 to 70 events per hour were reported. The 1999 SAP recommended the use of the 90th percentile value of 20 events. A mean of 9.5 events was also reported by Reed, which is similar to the mean reported by Zartarian et al., 1995 and 1997 using similar video tape techniques while observing 4 farm worker children (2-4 years). The mean is considered applicable to longer-term exposure estimation.

7. Page 7, 5th Paragraph, Line 2: In order to reduce potential exposure, Syngenta agrees with the EPA's recommendation to require label language to prohibit application of the granular formulation by hand or with hand-held devices, i.e., belly-grinder, and to strengthen wording to prevent accidental ingestion by children. The need to water-in following application should also be emphasized on the labels; incidentally, these are not Syngenta labels.

HED Response: [None required] The Agency is encouraged by Syngenta's interest in product

stewardship.

8. Page 14, "Methods and Types of Equipment used for Mixing, Loading, and Application", Line 5: The confusion regarding the terminology "truck-mounted sprayer exposure" is unclear. The typical definition of this is a groundboom sprayer. The data in PHED clearly covers this type of use pattern.

HED Response:
The truck-mounted sprayer is generally referring to roadside or rights-of-way sprayers.

9. Page 27, 4th bullet, first point: If aerial short-term risks are assessed using1,200 acres sprayed per day, no intermediate-term risk assessment (greater than 30 days/year) should be calculated. The EPA scenario that one aerial applicator and loader would treat a minimum of 36,000 acres (1,200 acres per day x 30 days) of corn per year is implausible. Doane Marketing data show that in 1999 and 2000, only 4 states out of 16 that used atrazine had more than 50,000 acres of corn aerially applied with atrazine during a one year period. It is not realistic that one individual person applied atrazine over all the aerially-treated corn acres within one state, so the intermediate-term risk assessment using 1,200 acres/day needs to either be removed or the acreage adjusted to reflect real-word practices. See comment 15 below.

HED Response:
This point is well made, mathematically. Also, the acreage information agrees with USDA and BEAD data. Therefore, it is unlikely that the highest acreage would be applied for more than 30 days and intermediate-term exposure estimates will not be calculated in the revised document for the highest acreage for these scenarios.

10. Page 28, 3rd item: The assumption that 960 tons of bulk dry fertilizer is impregnated with atrazine per day is incorrect. The correct assumption would be 200 tons of fertilizer per day. Data supporting this assertion is found in Appendix 3 of this Attachment. The exposure assessment should be revised accordingly.

HED Response:
The figure of 960 tons treated per day is based upon facility capacity, from various data sources, and therefore appropriate for use for this deterministic daily maximum exposure estimate and comparison to a short-term toxic dose. Syngenta's estimates are based on typical usage information, which is useful in characterizing the probability of mixing fertilizer with atrazine for eight hours per day. However, because the Agency is not assessing chronic handler exposure from treating fertilizer, a probabilistic analysis using average or typical quantities handled is not appropriate. Because the information provided is considered more specific to atrazine applications, it was used, *in toto*, to estimate a reasonable maximum commercial treatment rate of approximately 500 tons. Therefore both 500 tons and 960 tons per day were used in the revised assessment to provide a range of exposure estimates for risk management decisions.

11. Page 28, 4th item: It is unclear how EPA arrived at a range of 143 to 500 acres treated per day with granular fertilizer. Information from equipment manufacturers indicate that 120 acres/day is a more realistic number. This is based on a typical truck capacity of 10 tons (20,000 lbs) with an application rate of 500 lb fertilizer per acre. With each truck load capable of treating 40 acres, a typical day would consist of filling the truck 3 times for a total of 120 acres/day. Acreage treated is limited by truck/hopper capacity, swath width, surface conditions, and fertilizer application rate.

HED Response:

Initial HED estimates were based upon technical feasibility, rather than actual practice data. According to specifications for drop-load tractor drawn equipment, up to 500 acres per day may be treated at the rate of 200 lbs fertilizer/acre. The average farm (USDA) has about 150 acres in corn, and most have less than 500 acres. Syngenta has provided several sources of information which help to characterize practices in the field. Follow-up inquiries performed by scientists in the BEAD confirm that most treated fertilizer is mixed, loaded and applied by custom operators in the Midwest; and that fertilizer is applied directly to the fields by trucks with spinning disk type spreaders, at a rate of approximately 160 acres per 10-ton truck per day (4 trips at 40 acres each) or twice as much for a 20-ton truck. Therefore, the applicator exposure to treated dry fertilizer will be re-estimated based on this updated information.

12. Page 28, 5th item: The default assumption that professional LCOs spray 5 acres per day is in error and should be replaced with an assumption of 3 acres per day as has been previously used by the Agency during the RED process and supported by the ORETF data. The data provided by ORETF supported 2.5 acres treated per day by LCOs as a high-end estimate, not 5 acres. For an upper-bound estimate of area treated and to be consistent with previous Agency risk assessments for other turf products, the default assumption of 3 acres per day should be used.

HED Response:
The HED has presented estimates of both 3 and 5 acres in some assessments, where there are data on use-specific acreage. While the ORETF recommends 2.5 acres per day as "typical" for lawn care operators, five acres is within the capability of these operators for a full 8 hour day.

13. Page 28, 2nd bullet point, Line 4: PHED data, ARTF data and ORETF data as well as proprietary studies show that the protection factor of a layer of clothing is much greater than the 50% used by EPA. Data from these sources show that clothing provides approximately an 80% protection factor. The EPA response to Syngenta's 30-Day Comments indicates that the Agency is in the process of considering data on this issue as part of ongoing NAFTA harmonization. For transparency please provide a list of the data under evaluation.

HED Response:

The amount of protection afforded by personal protective equipment (PPE) and clothing has been

studied and discussed in many venues. There is a wide range of reported protection factors in the literature. The type of clothing worn, activity, application method, formulation of pesticide, and the individual's work behaviors all affect the protection level. For example, coveralls generally afford less protection from overhead spraying in a greenhouse than from application of granular formulations. In general, it is the HED policy to assign a protection factor (PF) of 50% for the covered body part (for coveralls this would exclude hands, feet, and head) for each additional layer of clothing, and a 90% protection factor for the hands for chemical-resistant gloves. Due to the wide variation in types of materials available, coveralls are assumed to be made of permeable fabric unless chemical and fabric-specific penetration data is available. Based on this formula, the HED's use of a 50% PF for coveralls on top of a single layer of clothing generally represents more than a 75% PF for the body (0.5 x 0.5 = 0.25 x total exposure). The PHED and ORETF databases use actual data for most of the surrogate exposure scenarios.

HED does not currently have a policy for the use, or the protection factor afforded by, chemical-resistant protective clothing or head gear. It is obvious that impermeable materials afford more protection than permeable coverings, but, as with gloves, the penetration rate is related to the chemical, material, application method, and duration of exposure. HED is currently working with the NAFTA task force to harmonize various standard assumptions, and protective clothing is one of the topics. In addition to a lack of data, HED has concerns about the proper selection and use of chemical protective clothing (CPC) in general agriculture. The use of CPC carries a potential risk to the wearer of hyperthermia and dehydration. Therefore, as with respirators, the more highly protective the clothing, the less "breathable" and more cumbersome they are. The CPC may introduce a hazard into the work place, so again, a program including training, medical clearance, CPC selection, and equipment maintenance is necessary. Because of the many drawbacks to using PPE, the HED encourages the use of administrative and engineering controls whenever feasible.

14. Page 29, 2nd paragraph: The parameters used in the impregnation of dry bulk fertilizer scenario by EPA are incorrect. This is a closed system process that occurs only in commercial fertilizer plants. A description of the process along with the risk assessment can be found in Appendix 3 of this Attachment. The exposure assessment should be revised accordingly.

HED Response:
The HED, with corroboration from BEAD, concurs that nearly all impregnation of dry bulk fertilizer is performed in commercial plants. Label language should be changed to clarify this intention. Syngenta conducted a study of seed treatment in Canada, which has been reviewed by HED/Health Canada in a separate memo. These data were found to be of sufficient quality and more appropriate for use in estimating the loader/operator exposure in commercial fertilizer admixture plants. The exposure estimates will be updated accordingly. However, the daily bulk treatment rates cited by Syngenta may be typical but are not appropriate for a short-term risk estimate (see response to Comment # 10).

15. Page 34, 1st paragraph, Line 3: It is stated that the intermediate-term exposures may be refined as more atrazine-specific use data becomes available. The following are the aerial

scenarios where intermediate-term risks were less than 100:
Mixing/loading liquid and DF formulations for aerial application:
- sugarcane (2.6 and 4 lb a.i./A, 350 acre)
– Christmas trees (350 acre)
- sod farms (350 acre)
– conifer forests (4 lb a.i./A, 350 acre)
– chemical fallow (3 lb a.i./A, 350 and 1200 acre)
– chemical fallow (1.4 lb a.i./A, 1200 acre)
– CRP and grasslands (2 lb a.i./A, 1200 acre)
– corn and sorghum (1 and 2 lb a.i./A, 1200 acre)
Information regarding yearly aerial application of atrazine to sugarcane, corn, and sorghum indicate that the daily acreage assumptions used by EPA are not feasible when extrapolated to a period of 30 days. Thus, either the daily acreage assumption is incorrect or the assumption that spraying takes place for a period of more than 30 days per year is incorrect. Information obtained from Doane Marketing show that the latter is the case. Actual use of atrazine in aerial applications was determined for sugarcane, corn and sorghum utilizing Doane Marketing Research, Inc. The crop rate and acreage scenarios were expanded to show the total number of pounds active ingredient and acres for 30 days that the individual mixer/loader would have to complete to meet the scenario limits. The Doane database was queried for atrazine active ingredient applied by air, and the number of pounds and acres at the state level for the years 1999 and 2000 (Appendix 4 of Attachment 5, Table 1). From these values, the average pounds active ingredient per acre by state could be calculated. Unless the 30 day combination of total pounds, acres, and lbs ai/A were met within a state, there is no possibility of an individual handling enough product to reach the unacceptable intermediate-term risk scenario.
Sugarcane: Only LA showed any aerial application data. The scenario number of pounds applied (350 acres/day x 30 days x 2.6 lb a.i. /A = 27,300 lb a.i.) was not reached, and the calculated number of treated acres (350 acres/day x 30 day =10,500 acres) was not met in 1999. While the number of acres was met in 2000, the average application rate of 1.67 lb a.i./A was below that specified, 2.6 and 4.0 lbs. a.i./A, in the exposure scenario. Thus the sugarcane criteria were not met even if one mixer/loader serviced the entire state. Please revise the risk assessment accordingly.
Corn: the exposure scenario specifies 1.0 and 2.0 lb a.i./A on 1,200 acres per day, or 36,000 to 72,000 lb ai, and 36,000 acres. In the entire U.S. for the years 1999 and 2000, the number of pounds of aerial atrazine per year reported by Doane ranged from 435,000 and 187,000 and the acres between 435,000 and 220,000. Aerial application was reported in only 16 states, with considerable annual variation. The states of KS, NE, OK, and TX were the only ones exceeding 50,000 acres per given year. Also, most annual average rates per acre were less than 1.0 lb a.i./A per given state. Since it is highly unlikely that one mixer/loader services the whole state, any given individual would not have handled the quantity of atrazine specified in EPA's intermediate-term exposure scenario. Please revise the risk assessment accordingly.
Sorghum: the exposure scenario specifies 1.0 and 2.0 lb a.i./A on 1,200 acres per day, or 36,000 – 72,000 lbs and 36,000 acres. In the entire U.S. for 1999 and 2000, the number of pounds of atrazine applied aerially ranges between 390,000 and 450,000 lbs and the acres range between 340,000 and 300,000. Aerial applications occurred in 1999 and 2000 in seven sorghum growing

states, with considerable annual variation in acres treated. Of these, there were only two states (TX and NM) in which the amount of atrazine applied by air exceeded what the EPA model predicted for one mixer/loader. Since it is highly unlikely that one mixer/loader is servicing the entire state, the chance of any given individual meeting the intermediate-term scenario is remote. Please revise the risk assessment accordingly.
Doane does not have survey data from other uses in the list including CRP/grassland, Christmas trees, sod farms, conifer forests, and chemical fallow, but the relative use of atrazine on these sites is minor when compared to the crops discussed above.
There is another aspect of the scenario that needs to be examined. This involves the number of 2.5 gallon jugs handled within an 8 hour day to meet the scenario specification. Table 2 in Appendix 4 of Attachment 5 shows in detail the various crop risk scenarios, the daily maximum number of pounds, number of 2.5 gallon jugs to provide those pounds, required jug rinses (as directed on the AAtrex 4L label), the calculated number of minutes per jug, and an estimation of whether this is physically possible for 8 continuous hours. The estimate is just for the jug handling, and does not allot time for retrieving material and filling the aircraft with water. For Christmas trees and sod farms, which did not list an application rate, the labeled maximum of 4 lb a.i./A has been used for the calculations. The 2.5 gallon container holds 10 lb atrazine (2.5 gal jug x 4 lb a.i./gallon = 10 lb a.i. per jug). Across the crops/sites of concern, the pounds of atrazine needed per day ranges from 1,400 to 3,600. The poundage range would thus require 140 to 360 2.5 gallon jugs per 8 hour day. On an hourly basis, the mixer/loader would have to empty ~17 to 45 jugs per hour. The AAtrex label specifies under Container Disposal: "Triple rinse (or equivalent) and offer for recycling or reconditioning,……". In addition to the initial emptying of each jug containing AAtrex 4L, the mixer must rinse (3X) each jug to meet label requirements. Thus, in addition to the 17 to 45 jugs of AAtrex 4L to empty per hour, the individual would also have to rinse the jugs. The physical impossibility of this open loading system needs to be considered.

HED Response:
Based on information provided by Syngenta, and the BEAD and other sources, it is unlikely that any single applicator makes the maximum acreage aerial application more than 30 days per season. Given the widespread use of atrazine, however, intermediate-term exposures from handling lesser amounts of atrazine are possible. Table 7 of the Occupational and Residential Exposure Assessment shows the exposure and risk estimates for mixer/loaders for aerial applications using engineering controls. The data submitted on application rates and acreage treated will be considered in the revised exposure assessment, and the highest daily acreage will be considered to be a short-term exposure. Ergo, the maximum daily aerial or ground acreage were not used for intermediate-term exposure scenario assessments.

16. Page 38, 2nd item: The mixing/loading and incorporating liquid atrazine into dry bulk fertilizer does not take place on farms. This reference should be removed. Syngenta has submitted a document (Appendix 3 of Attachment 5) that details the herbicide/fertilizer application process so that the risks can be more accurately assessed.

HED Response:

The HED acknowledges that bulk impregnation of fertilizer with atrazine is less likely to occur on-farm. There is no label restriction to prevent such use, however. Therefore a screening risk estimate using open mixing, loading and application to an average size farm has been done. See also response to Comment # 14.

17. Page 38, 3rd item: Exposure data for granular ground application from data in PHED can be used to assess exposure to workers applying granular atrazine impregnated fertilizer to soil. The data in PHED are generic and can be used as surrogate for many different active ingredients as long as the formulation is constant.

HED Response:
In Tables 6 & 7, Scenario 8 of the Occupational and Residential Exposure Assessment, HED used PHED to determine that application of atrazine-impregnated fertilizer at the highest estimated rates results in MOEs greater than 100 with additional PPE or engineering controls (closed-cab truck).

18. Page 38, 7th item: In the review of handler studies incorporating biomonitoring [Study submitted to the Agency in several phases including interim reports, final reports, and amendments are given MRID 439344-17, 439344-18, 441521-09, 441521-11, 443154-03, and 44154-04.] EPA cites two issues related to this study (see below). Based on the information and references in Syngenta's comments (also below) these issues should be resolved and the statement regarding low confidence removed from the risk assessment.
EPA Statement
"Another significant issue was the choice of urinary total chloro-triazine residues for biological monitoring. The chloro-triazine residues represent only 12% of the total atrazine dose. It is HED policy that the predominant metabolite be used as the indicator for calculating the parent chemical, thereby reducing the error potential when back-calculating the dose."
Syngenta Comment
There is general agreement that atrazine and its chloro-triazine metabolites are the moieties of toxicological concern (MARC 1). Furthermore, Syngenta has established a relationship between administered dose and eliminated dose in the human oral dose study on atrazine 2 . In this study, it was determined that approximately 12% of the chloro-metabolites were eliminated in the urine. Thus, by directly measuring the moieties of toxicological significance, the back-calculated input dose of atrazine is not a critical feature of this assessment. This method was utilized mainly to permit a comparison of the biomonitoring results with whole body dosimetry and the Pesticide Handlers Exposure Database. The general concordance of these three independent methods for estimating the atrazine exposure provides the reviewer a level of assurance that the estimates from all these methods are likely to be correct.
EPA Statement
"Also, urine creatinine and creatinine clearance were not measured. Without these measures, there is no way to verify the accuracy of the volume of urine collected during biomonitoring (which is critical to calculating the total dose absorbed)."

Syngenta Comment
Urinary creatinine/clearance are parameters to measure if only a partial sample of the daily urine output is collected, i.e., first void. In this agricultural handler study 3 , total daily urine outputs were collected, making creatinine correction for volume unnecessary. The usefulness of creatinine data has been a subject of much debate and is, in fact, described in the EPA Series 875.1500 as only a procedure the investigator should consider as a way of monitoring completeness of collection. This does not indicate in any way that this data is necessary for data evaluation or that it is critical to the study design.

HED Response:

Conjugation and dealkylation of atrazine result in the primary metabolites, several chlorotriazines and atrazine mercapturate. Chlorotriazines account for 14% of the human atrazine dose when measured over seven days after exposure. There were no data available on human excretion rate of the mercapturate. However, two separate methods were proposed by M. W. Cheung in 1998 for Ciba Crop Protection for biomonitoring of atrazine metabolites: measuring chlorotriazines and atrazine mercapturate. An ELISA method was proposed for the mercapturate. According to the Ciba worker biomonitoring study, availability of a rapid, reliable, and economical immunochemical test for the metabolite of interest was a decision factor in the choice of the metabolite measured. Rat and monkey studies quantified the excretion of chlorotriazine and mercapturate metabolites of atrazine. Given that a human oral atrazine excretion study is available, the chlorotriazine metabolites are acceptable for use in quantifying exposure. Exposure estimates must be adjusted for dermal absorption.
While EPA acknowledges that creatinine measurements are corroborative, there were inconsistencies and design problems in the study which create uncertainty as to the correlation between biomonitoring data and amount of chemical handled. Because urine biomonitoring was being performed in the midst of application season, workers were exposed on more than one day, while atrazine is excreted over several days, further complicating a correlation of dose to quantity handled. Please reference the review of the biomonitoring studies in the section titled **Agricultural Handler Study Summaries**: Handler studies incorporating biomonitoring, approximately pages 18-24 of the Occupational and Residential Exposure Assessment:

"As indicated by the amounts handled per day, the dose was not found to be "steady state," as suggested by the authors. Also, due to collection of 24 hour urine samples during the spray season, it was not possible to determine the relationship between the amount handled on a given day and the chlorotriazines excreted the following day. The mean 90th percentile daily dose was selected to represent a daily dose for each category. This is considered a reasonable, yet high daily value as the study monitored actual work practices without influencing amounts of atrazine handled. The HED calculation showed internal doses of 0.012 mg/kg/day for mixer loaders, 0.0038 mg/kg/day for applicators, and 0.014 mg/kg/day for mixer/loader applicators. These doses are within the same range as the study findings. The HED calculation is only approximate, however, because during the study, atrazine was handled on consecutive days (or not at all), and atrazine is excreted in the urine in quantifiable amounts for at least 3 days after exposure. Some of the highest daily doses were based on days when little or no atrazine was handled. Therefore,

there is both the "lag time" to excretion, and the additive nature of consecutive daily doses. Use of the single 24-hour excretion correction of 12% for chlorotriazines does not correct for either of these major confounding factors. Atrazine metabolites continue to be excreted for several days after exposure, so measuring the daily excretion only provides data about the body burden at that time. Therefore, for the purpose of interpreting this study, the mean to 90th percentile of the maximum doses are considered most representative for each job category for calculating MOEs for handlers."

19. Page 39, Post application Exposure Scenarios: Although the EPA has acknowledged that atrazine is applied during the "dormant" months to conifer tree farms when staking and shaping are not done, the risk assessment calculation has not been removed from EPA Table 12. Please revise the risk assessment accordingly.

HED Response:

Because of the timing of application and the fact that the treatment is directed at the ground beneath the trees, staking and shaping activities are unlikely to result in atrazine exposure and will be removed from the revised assessment. Scouting activities are still considered likely and will be included.

20. Page 30, Post application Exposure Scenarios: Although the EPA has acknowledged that harvesting sod would not occur within the 30-day pre-harvest interval in Florida and other states, it is still part of the risk assessment presented in EPA Table 13 and should be removed.

HED Response:
Not all states have a 30-day pre-harvest interval. However, the Agency has made inquiries to several experts who confirmed that herbicide use close to harvest date is unlikely for economic reasons, and also because residual herbicides reduce rooting-in of sod once it is laid on the new site. Therefore, the Agency agrees that manual activities associated with harvesting sod are unlikely to take place within the 2-3 weeks after application when detectable residues are present, and residential contact with treated transplanted sod is less likely. Mechanical mowing will still occur, but exposure to atrazine residues during harvesting would likely be only at a reduced level, therefore the assessment for short- and intermediate-term exposure scenarios will be adjusted accordingly.

21. Page 43, 1st bullet item: It is scientifically inaccurate to compare the toxicity endpoint from a long-term toxicity study to exposure based on foliar residues found at 7 days after an application. The time periods are not similar. Since the intermediate-term re-entry risk assessment is designed to evaluate risks to workers handling atrazine-treated crops for periods longer than 30 days, the residues at 30 days, or more, after an application should be used. Please revise the risk assessment accordingly.

HED Response:

Intermediate-term (more than 30 days) postapplication exposures are considered less common than short-term exposures to atrazine-treated foliage. However, there is insufficient data to conclude no intermediate-term exposures to atrazine residues occur. It would be more appropriate to use longer-term residues (30 days) for intermediate-term exposure estimates, but the corn DFR study data available terminate at the 7th day. Because all risk estimates based on exposure to 7th-day residues did not exceed the level of concern for workers, and the estimates are considered to be adequately protective, further extrapolation of the residue data was not necessary. The geometric means of the actual DAT 0-35 residue data for granular formulations and the predicted DAT 0-31 residue data for liquid applications were used in the updated exposure assessment.

22. Page 44, 3rd paragraph: On page 39 it was acknowledged that turf (sod) harvesting would not occur within 30 days of an atrazine application; however, a harvesting risk assessment was performed (Table 13) and summarized. This exposure scenario should be removed.

HED Response:
See response to Comment #20.

23. Page 44, 4th paragraph, Line 3: On page 39 it was acknowledged that harvesting of Christmas trees does not take place during the same time period as an atrazine application; however, the harvesting risk assessment was performed (Table 12) and summarized. This exposure scenario should be removed.
The staking of Christmas trees is not done. Several prominent university personnel were contacted to obtain localized information as to cultural practices and determine if staking of Christmas trees is a normal cultural practice. Their comments follow:[*see full original Syngenta text*]
All of these experts agreed that such a scenario does not occur. Syngenta thus requests that this scenario be removed from the risk assessment.

HED Response:
According to the considerable expert testimony provided by university professors on the topic, atrazine is generally applied to Christmas trees in the spring, and only in the Northwest states is it applied by aircraft, usually helicopter. Generally speaking, the experts agree that "trimming or shearing of the tree's new growth is done after mid-July, when annual growth is complete," and staking is never done. It is logical that ground equipment would direct the spray to avoid tree roots and foliage as much as possible, as per Syngenta testimony. Also, Christmas trees are a multi-year crop, so the less inputs the better for the grower. Based on the information provided, with concurrence by agricultural experts in HED and BEAD, and known atrazine dissipation rates, a postapplication Christmas tree worker exposure assessment is no longer required and will be removed from the revised assessment.

24. Page 47, 5th bullet item, Line 4: Syngenta supports the use of label language on consumer products to prohibit hand spreading of granulated product.

HED Response:
HED agrees with the comment, no response required.

25. Page 49 last bullet item: Syngenta supports the use of label language on consumer products to prohibit hand spreading using hand-held spreaders of granulated product and will work with EPA to ensure that this label restriction will be added to all consumer labels for products containing atrazine.

HED Response:
HED agrees with the comment, no response required.

26. Page 50, 4th bullet item: According to discussions on March 21, 2001, between the ORETF and representatives from EPA, it appears that the review of the ORETF mixer/loader/applicator monitoring data is complete and these data are viewed as high confidence. Therefore the statement "The data from the ORETF studies has been classified as medium-to-high confidence level"is incorrect and should be revised.

HED Response:
The Atrazine Risk Assessment will be revised and appropriate updated language added to reflect the final review of the ORETF studies.

27. Page 50, Postapplication Exposure Scenarios: The statement that duration of postapplication dermal exposure is expected to be either short-term or intermediate-term is incorrect. It contradicts what is stated three sentences later in the same paragraph: "it is not expected that individual residential exposure duration would exceed 30 days in duration." Please correct.

HED Response:
The text has been corrected to state that intermediate-term residential postapplication exposures are not anticipated.

28. Page 51, Summary of Postapplication Spray Drift/Track-In Risks: This is a new risk assessment category that is not in the publicly available 1997version of the EPA Residential SOPs. Although Syngenta recognizes that there exists some preliminary research data in this area, we remind the Agency that it should provide an opportunity for the scientific community to fully evaluate the findings from these studies and to discuss how to form a generic regulatory risk model.

HED Response:
Comments are accepted. Spray drift is always a potential source of exposure to residents nearby to spraying operations. This is particularly the case with aerial application, but, to a lesser extent, could also be a potential source of exposure from groundboom application methods. The Agency has been working with the Spray Drift Task Force, EPA Regional Offices and State Lead Agencies for pesticide regulation and other parties to develop the best spray drift management practices. The Agency is now requiring interim mitigation measures for aerial applications that

must be placed on product labels/labeling. The Agency has completed its evaluation of the new data base submitted by the Spray Drift Task Force, a membership of U.S. pesticide registrants, and is developing a policy on how to appropriately apply the data and the AgDRIFT computer model to its risk assessments for pesticides applied by air, orchard air blast and ground hydraulic methods. After the policy is in place, the Agency may impose further refinements in spray drift management practices to reduce off-target drift and risks associated with aerial as well as other application types where appropriate.

29. Page 52, 2nd paragraph, Line 4: Delete the words "…and intermediate-term (DAT 7)…" as this scenario is no longer applicable.
Page 52, 3rd paragraph: Syngenta has provided information on granule size distribution for consumer products containing atrazine. The statements that "the 'weed and feed' (fertilizer/herbicide combination) granules would be considered more attractive and more likely to be consumed if readily visible and easily picked up by a child" and "the granular product was described by Scotts as having the size of 'beach sand'" are misleading. Syngenta atrazine is only sold in combination with fertilizer ("weed and feed") for consumer use on lawns. As noted in the document prepared by Syngenta (Appendix 2 of Attachment 5), the granule size and percent of granules by size varies by manufacturer.
The statement that less than a teaspoon of atrazine-containing fertilizer would exceed the toxic level of concern is scientifically unsubstantiated and very misleading. The amount of atrazine-containing fertilizer granules in a teaspoon is highly dependent on the size of the granules; thus it is possible that a teaspoon of large granules would not exceed the toxic level of concern.
The other point that must be considered for this type of a risk scenario is the availability of the granules. The granules are so small and the percent of atrazine in the product so low, that a child would have to pick out approximately 200 granules from a lawn to consume enough atrazine to provide the dose calculated by EPA. Please revise the risk assessment accordingly.

HED Response:
The text has been corrected to indicate that all residential exposures are anticipated to be short-term (less than 30 days). Based on the information supplied by Syngenta with their comments, 5 of 8 products were composed primarily (>50%) of granules of greater than 2 mm diameter. These granules are, by Syngenta's description, large enough to be seen and possibly picked up by small children. It would take between 10-20 of such granules to make up the 0.4 Gm of product assumed in the Residential SOPs. The HED scientists, using best available data, consider 10-20 granules to be a high-end estimate for small children, but appropriate for screening incidental exposure. Refinement of the Residential SOPs is expected as more data becomes available on hand-to-mouth exposure. Syngenta's planned study of hand-press granular exposures may be applicable to this assessment.

30. Page 55, 1st Paragraph: The "hand-licking" risk model has not been adequately peer reviewed and should not be included in any assessment until properly evaluated and data availability and needs are understood. There are no data to presume that results from a corn dislodgeable foliar residue study in any way represent transfer of pesticide residues from turf to a child's moist hand, so the corn DFR value should not be used to justify the 5% transfer factor. The default 5%

transfer rate should in fact be replaced by the actual turf transferable residue data for atrazine adjusted for wet hands. As seen in the Clothier (2000) study, a 3-fold increase in wet-versus dry-hand transfer should be used until more relevant data are developed for this scenario in turf. When the TTR data for granular atrazine are multiplied by a factor of 3 and then placed into the model, the "hand-licking" risks are acceptable. Based on the large TTR data sets submitted to EPA by the ORETF as well as proprietary turf studies submitted by Syngenta, it is apparent that the transferability of liquid pesticides is significantly greater than that of granular pesticides. That difference in transfer is not taken into account in the EPA "hand-licking" model. Please revise to take this difference into account in the assessment. This revision does not reflect Syngenta's agreement that the "hand-licking" model is valid or realistic.
It is clear that the "hand-licking" model being used by EPA for regulatory decisions needs further validation. Until that has been done, it is inappropriate to use this model for regulatory decisions.

HED Response:
See response to Comment #3.

31. Page 55, 3 rd Paragraph: The use of data from a corn foliar dislodgeable residue study to reflect how much residue a child may remove when mouthing treated turf or bringing an object to the mouth is speculative. The model should be validated prior to being used in regulatory risk assessments.

HED Response:
The document has been revised using the Recommended Revisions to the Standard Operating Procedures (SOPs) for Residential Exposure Assessments (2/20/01) in lieu of the foliar data. The TTR data were not used for reasons explained in the Recommended Revisions to the SOPs, SOP # 2.2. (See response to Comment #3)

32. Page 57, 1st bullet item: Remove the words "and intermediate-" as the risk assessments are for short-term risks only.

HED Response:
The text has been corrected accordingly.

33. Page 57, 3rd bullet item: As noted previously, there has been no relationship developed to correlate the data from a corn dislodgeable foliar residue trial to how much pesticide residue can be transferred from treated turf to a child's hand.

HED Response:
See response to comment #31.

34. Page 57, 5th bullet item: The statement that "atrazine TTR study data indicate transferable residues are greater after the day of application" contradicts the TTR data presented in EPA Table 11. The highest residues in three of the four sites were seen at 12 hours after the

application; at the fourth site, the highest residues were seen at the sampling immediately following the application.

HED Response:
To be precise, the data shown indicate some residues increase from 4 to 12 hours before decreasing (both liquid and one granular formulations). This clarification has been included in the revised exposure assessment.

35. Page 57, 6th bullet item: This bullet should be removed since all residential risk assessments were for short-term exposure only.

HED Response:
The text has been corrected accordingly.

36. Page 57, 2nd paragraph, Line 8: As noted previously, the arbitrary aggregation of three activities with atrazine-treated turf – golfing on atrazine-treated golf courses, mowing atrazine-treated grass, and "high-contact activities" on atrazine-treated grass – is not realistic nor an approved regulatory scenario.

HED Response:
See response to Comment #1.

37. Page 57, last paragraph/page 58, first paragraph: The same-day aggregation of applying atrazine to a half-acre lawn and then playing on the treated lawn for 2 hours is not realistic nor an approved regulatory scenario. Both individual exposure scenarios are based on conservative, high-end parameters, and it is, therefore, inappropriate to add these screening-level point-estimates together. Syngenta is unaware of any published EPA policy or exposure assessment guideline which states this aggregation as "a high-end, screening level exposure estimate" and request a copy of this policy.

HED Response:
See response to Comment #1.

38. Pages 58, 2nd paragraph: There are no data to presume that residues from a corn dislodgeable foliar residue study represent transfer of pesticide residues from turf to a child's moist hand. However, in the interest of presenting a calculation of this type of scenario, the default 5% transfer rate should be replaced by the actual turf transferable residue (TTR) data from the atrazine turf study and adjusted for wet hands. As seen in the Clothier (2000) study, a 3-fold increase in wet- versus dry-hand transfer should be used until more relevant data are developed for this scenario in turf. When the TTR data for granular atrazine are multiplied by a factor of 3 and then placed into the model, the "hand-licking" risks are acceptable. Based on the large TTR data sets submitted to EPA by the ORETF as well as proprietary turf studies submitted by Syngenta, it is apparent that the transferability of pesticides from turf is dependent on whether the formulation is granular or liquid. This difference in transfer based on formulation is not

taken into account in the EPA "hand-licking" model.

HED Response:
See response to Comments # 3, 31. The difference in transfer rate based on formulation has not yet been incorporated into the Residential SOPs.

39. Page 58, Aggregate Exposure Estimates, 1st paragraph: The arbitrary aggregation of all potential activities that a person may do in an 8 hour period on a pesticide treated lawn (4 hrs of golf + mowing 2 hrs + 2 hrs of high-contact activity) immediately following an application is unfounded and unreasonable. There are no activity pattern data to form a basis for such a risk assessment nor is this type of risk manipulation sanctioned in the EPA Residential SOPs.

HED Response:
See response to Comment # 1.

40. Each one of these individual risk assessments are based on upper-bound assumptions and contain a bias towards conservatism; the addition of these individual risks results in exaggerated exposure estimates that are of little value in terms of assessing true risk. This specific aggregate methodology is not scientifically valid and should be removed.

HED Response: It is generally not necessary to aggregate risks where one route of exposure results in a risk which exceeds the level of concern. The aggregate in this case simply demonstrates which exposures are driving the risk equation, i.e., hand-to-mouth.

41. Page 59, Summary of Postapplication Risk Concern, 2nd paragraph: As mentioned previously, Syngenta ascertains that the hand-licking model has not been validated. Syngenta has prepared a document that describes the size characteristics of atrazine-impregnated granular fertilizer used on residential turf as well as grass morphology; this information provides additional evidence that ingestion of granules is not a likely actual event and should be removed from this assessment.

HED Response:
See response to Comment #3. The Syngenta information, as well as other chemical studies, consistently show that granular formulations have less residue than wet applications, but the degree to which this can be factored into the hand-to-mouth exposure equations has not yet been determined.

42. Page 59, Data Gaps and Uncertainties, 2nd bullet item: The statement that the TTR studies were conducted without watering-in is incorrect; the granular turf study (MRID 449588-01) had both non-irrigated and irrigated plots. The impact of irrigation on residues and potential exposure should be presented.

HED Response:
The effects of irrigation were mentioned in the study summary and briefly in summary, but will

be clarified in the text and the erroneous statement changed. The exposure assessment will be corrected to reflect the irrigated turf data and the effect of irrigation. After irrigation, at 12 hours postapplication, the mean TTRs were 0.012 µg/cm2 at the Georgia site and 0.074 ug/cm2 at the Florida site. There is a 2-4 fold lower TTR on irrigated grass compared to non-irrigated grass. The effect of irrigation is therefore very significant and watering-in should be required on the label to decrease potential exposure.

43. Page 59, Data Gaps and Uncertainties, 4th bullet item: Data on granular size and product breakdown has been generated by Syngenta and submitted to EPA. Turf residues following irrigation is available to EPA in the submitted granular TTR study (MRID 449588-01).

HED Response:
The HED gratefully acknowledges receipt of the data on granular size and product breakdown, and the post-irrigation residue data in MRID 449588-01. These data were included in the revised exposure assessment, and the reduced exposure associated with post-irrigation treated turf was also described.

44. Page 59, Recommendations: Syngenta agrees with EPA that probabilistic approaches help refine risk estimates. Because a policy on the development and use of probabilistic non-dietary risk assessment has not been issued, additional discussions on data sets and methodologies are needed.

HED Response:
The HED agrees with the comment.

45. Table 6: As mentioned previously, some of the scenarios assessed for intermediate-term risks should not be calculated as it is not possible to treat at the daily acreage assumed when extrapolated to a period of 30 days or more.

HED Response:
See response to Comment # 15.

46. Table 6: Mixing/Loading Liquid Formulations for Lawn Handgun Application (LCO) – the assumption that 100 acres of lawn and/or golf course will be treated with a hand-gun appears to be erroneous. Using the EPA assumption that a typical LCO treats 5 acres of turf per day, this mixer/loader is loading 20 vehicles with atrazine in one day for the short-term risk assessment, and loading 20 vehicles per day for 30 days for the intermediate-term risk assessment. This is an overestimate of daily acres treated for short-term risks and the assumption that this could occur for 30 days out of a year is highly improbable.

HED Response:
Based on information supplied by the industry, and personal communications and site visits, a single mixer/loader may supply 20 trucks per day with various chemicals, including atrazine; each handler/applicator may easily apply 5 acres per day, or more. The probability that any one

person may handle atrazine daily for more than 30 days per season is unknown, but lawn care is considered to be an occupation more likely to have repeat exposures.

47. Tables 13 and 14: Footnote b – remove the example of Bermuda grass rights-of-way as this is not an appropriate example for a sod farm or golf course risk assessment.

HED Response:
The footnote example will be changed to reflect the more appropriate example of 4 lb ai/A for sod raised on Florida muck.

48. Table 17: footnotes d and e should be removed as there was no intermediate-term risk assessment done. The aggregate daily dermal risks for adults should be removed as this is not a standard approved risk assessment.

HED Response:
Footnotes d and e will be deleted from the revised document as there is no intermediate-term exposure assessment. As stated previously, while there is no standard method for combining risks, application and postapplication exposures, or high- and low-contact activities, can co-occur. Therefore, a qualitative description of these aggregate exposures has been included in the revised assessment.

49. Table 18: Footnote d – remove references to intermediate-term exposure and risk. Footnote e – remove reference to intermediate-term assessments.

HED Response:
Table 18 is now Table 17 and has been revised to remove references to intermediate-term exposures.

Response to Attachment 6, "Drinking Water Exposure Assessment for Atrazine and Various Chloro-triazine and Hydroxy-triazine Degradates", Groundwater

In response to Attachment 6 of Syngenta's Comments on the HED Human Health Risk Assessment for Atrazine and its Chlorotriazine Degradates, EFED scientists have reviewed the data from the following studies whose results were discussed in the comments contained in Attachment 6. Results from these two studies address the assessment of chlorotriazines in ground water:

> Syngenta/Community Water System Ground Water Monitoring Study for Atrazine and Its Major Degradation Products in Multiple States in the United States (MRID 453999-06)
>
> Re-Sampling of Domestic Rural Drinking Water Wells (MRID 455453-04)

In addition, some comments were submitted concerning atrazine Fate data.

Syngenta's Survey of Community Water Systems for Ground Water

Syngenta performed a "synoptic" survey of ground water designed to estimate the 95th percentile exposure from two strata of Community Water System (CWS) wells: those who had at least one positive value prior to 1998 (about 3% of wells in the PLEX system), and those with no previously detected values (about 97% of GW CWSs). Of the original 14,000+ GW CWSs in the PLEX database, 435 wells had at least one detectable atrazine sample from 1993 through 1998. 204 wells were selected from this first stratum, which served 1.99 million people. Of the remaining 14,115 CWSs serving 20.49 million people with no detected samples, 235 CWSs were selected.

The survey was designed with the goal of estimating the 95th percentile of the overall distribution of each stratum of CWS wells with a relative standard error of about 30%. Precision for any of the upper percentiles of the population, such as the 99th % (or upper 1%), is less good, with a wider interval around the estimate, and a lower probability of capturing the "true" proportion in any sample. As EFED discussed in previous meetings with Syngenta, HED and SRRD staff, a more desirable and protective goal for OPP is to estimate at least the 99th percentile of the population of wells and people exposed at that level, still a sizeable number of people. At EFED's request Syngenta ran the 99th estimates for the distributions of CWSs and of people served. The results were as follows:

Percentile Estimates for Atrazine and Metabolites in Groundwater CWSs[1]

Population of CWSs						
Atrazine "Detects" Stratum				**All CWSs**		
Atrazine		**Atz + Metabolites**	**UCL**	**Atrazine**	**Atz + Metabolites**	**UCL**
99th %ile	**1.53**ppb (93-98)	**1.90**ppb(c4)	#	**0.219**ppb	**0.561ppb**	**1.09ppb**
mean	**0.166**ppb	**0.427**ppb	**0.547**ppb	**0.0303**ppb	**0.120ppb**	**0.128ppb**

Population Served

[1] Several methods of data estimation were used, depending on the analytical method and the method of handling non-detect's. Individual cells reflect the highest value reported for that estimate, regardless of method.

Atrazine "Detect's" Stratum				Overall Population		
Atrazine		Atz + Metabolites	UCL	Atrazine	Atz + Metabolites	UCL
99th %ile	**0.75**ppb	**1.59**ppb	**1.67**ppb	**1.06**ppb	**0.621ppb**	**1.60ppb**
mean	**0.126**ppb	**0.326**ppb	**0.474**ppb	**0.036**ppb	**0.129ppb**	**0.150ppb**

For the population of CWS wells, the "atrazine detected" stratum had a 99th %ile of 1.90ppb atrazine+metabolites (no upper bound confidence interval was calculated) and a mean of 0.427ppb(u.c.i.=0.547ppb). Estimates for the distribution of people served were slightly lower. This stratum represents the approximately 3% of CWS wells expected to be higher in numbers of detected samples and sample values.

Estimates for the overall distributions of CWS wells and people are lower than those above because the small "detect" stratum is combined with the larger (~97%) stratum expected to contain mostly "non-detect" samples. The 99th %ile and mean population estimates for atrazine+metabolites were 0.621ppb (u.c.i=1.60ppb) and 0.129ppb (u.c.i.= 0.150ppb), respectively. Median sample values were non-detect in both groups except for one positve sample in the "detect" group, which gave the median result as 0.171ppb in the "detect" group only.

The highest sample value found was 10.8 ppb TCT for the "detect" group in a well that was taken out of service to be investigated for point source contamination. The second highest value was 2.34ppb. (Subsequent monitoring at another well in the same CWS as the highest well gave non-detectable residues.) Calculations were done both with and without those values.

Because this is a statistical survey, the one well with the high value of over 10 ppb for total chlorotriazines may represent other wells that can not be dismissed. Even if the well is taken out of service under suspicion of point source contamination, it remains representative of a situation and level that may be occurring in other GW CWSs. The distribution of values that contains this sample differs in the upper percentiles from the estimated distributions without it.

Syngenta did not calculate upper confidence bounds on some of the 99th %ile population estimates where they would extend outside of the sample data. This may be expected to happen in a number of cases, and for this reason and the above considerations the sample maximums were examined.

All sample values were below the DW Levels Of Concern. While there is still significant

uncertainty in estimating the upper percentiles of the "true" population of CWS wells and people served, the fact that detections comprised a small stratum of the population and that a large percentage (nearly 50%) of that stratum was sampled, gives support to the conclusion that exposure to atrazine and its metabolites from GW CWSs is low and limited.

Syngenta's Rural Well Survey and Resampling

In 1992-94 Syngenta did a survey of 1,505 private rural drinking water wells. Designed to represent a "high exposure" population, the wells were selected from areas of high atrazine use and conditions of suspected vulnerability due to soil conditions and well depth. One sample per well was taken/analyzed. Fourteen of these original 1,505 wells had either atrazine concentrations above the MCL of 3 ppb, or total chlorotriazine levels approaching or above the DWLOC of 12.5 ppb. The maximum sample contained approximately 20 ppb TCT. These 14 wells, and only these, were selected for resampling in 2001. The resampling results showed lower values, with all atrazine levels <MCL and all 14 TCT levels under the DWLOC of 12.5 ppb. Syngenta claims point source contamination for the original wells with high values and also cites karst conditions at these sites.

At least three of the 14 "resampling" sites sampled new wells, usually on the same property or relatively near the original well sampled, particularly if the original had been taken out of service. While all of these, again, were near the original "high" wells, the new wells represented some of the lowest values in the new sample. Some appeared to be constructed to much lower depths or to be better reinforced.

At other sites the records indicated that atrazine or other herbicides had not been used for varying amounts of time. These sites showed reductions from original levels, although all showed higher levels than those in the "new" wells constructed on other sites, regardless of the levels of the original sample.

Finally, where records had been kept for any sampling done between the original 1992-94 survey and the present one, levels were variable over the years, with some appearing to decline and others both rising and falling. No use records were available for these intermittent years.

One issue regarding the design of the rural well survey that EFED has pointed out previously is that only one sample was taken for each well. In earlier EFED comments and in discussions with SRRD, HED staff, and Syngenta, this issue was identified based on analyses of the ARP groundwater database. A limited scan of PLEX GW CWS data from the 1993 through 1998 period also provides examples of large variability from year to year in the sample data.[2] The data can show significant monthly variations, which clearly demonstrate that only one low detection

[2]PLEX data from White Hall, Ill., for example, show 5.3ppb(1993); 1.2ppb(1994); 10.0ppb(1996); and 7.0ppb(1997).

value for a well can not rule out the possibility of higher values at different times. For this reason it would be interesting to examine any resampling data Syngenta might have from other wells in the original Rural Well Survey, even if their original result was less than the MCL at the time.

Syngenta claims there is more spatial variation in the data than the temporal variation obvious in the ARP study. This may not always be the case, depending on the spatial and temporal sampling intervals in any given study. OPP would be interested in seeing Syngenta's data and analysis of the NAWQA studies regarding this issue. While it can be a matter of discussion as to which variability is greater in general, it is clear that both contribute to the uncertainty of the estimates, and the best sampling design would take into account some aspects of both spatial and temporal variability. The fact of only one sample per well for the RWS continues to contribute heavily to the uncertainty of any estimates made from these data.

Because the original sample was part of a survey of private rural wells, point source contamination suspected for any well in the survey might reasonably be expected to be occurring at some of the larger number of wells that each of these sampling units represents. Again, whether they are due to spills, misuse, or karst topography, the findings represent actual risks inherent in pesticide use. While it is gratifying that levels in the 14 wells were lower upon resampling, because only these wells were sampled, the possibility of high(er) concentrations in a larger, representative number of rural wells can not be ruled out. It is not clear where Syngenta's estimate of 30 rural wells over the DWLOC of 12.5 ppb derives from.

In addition, because the original Rural Well Survey was a sample of private rural wells, albeit one that was originally skewed for the purpose of providing an upper estimate of exposure, it represents a larger population of rural wells that serves a larger population of people. Syngenta should present the population(s) of people exposed to drinking water from private rural wells as part of its discussion. EFED agrees that this population is different from the population of GW CWSs.

Syngenta Comments on Drinking Water Estimates from Outside Major Use Area

Syngenta has obtained the SDWA data for 10 "minor use" states, representing additional area that brings the total usage area with data up to 99% from 90% (for "major use"). Although they claim that the number of CWSs with previous detect's is lower (on a percentage basis) in this use area compared with the same percentage in the major use area, actual levels are not discussed or summarized. OPP would like to see data from these areas of potentially higher-application minor use.

Syngenta Comment on Laboratory Soil Metabolism Half Life

This comment and others concerning atrazine Fate data is addressed in several documents of the EFED response. In one exercise EFED performed the PRZM/EXAMS model runs using Syngenta's suggested in-put values and no significant differences were found in the out-puts.

Response to Attachment 7, "Atrazine - Corn: Supporting Data for Amending Tolerances & Atrazine - Sorghum: Supporting Data for Amending Tolerances".

Responses based on a review of these data are contained in the responses to comments contained in Attachment 3 .

Response to Attachment 8, "Review of Atrazine Incidents Reports DP Barcode D270014".

The Syngenta company provided a response to the "Review of Atrazine Incident Reports DP Barcode D270014, Chemical #080803". The company's response comes from attachment 8 of "Syngenta's Comments on the EPA's January 19,2001 'Atrazine: HED's Revised Preliminary Human Health Risk Assessment (and associated EPA Documents) for the Reregistration Eligibility Decision (RED)" by Thomas Beidler, April 16, 2001, pages 318-323. This memorandum considers the issues raised in this response point by point. Syngenta's response is organized by introduction, consideration of each of the databases used in the review of incidents, and a conclusion. Each of these sections will be addressed, in turn, in the sections presented below.

Introduction

Syngenta comment: "The second sentence of the introduction states "USEPA consulted five separate databases for information on incidents that allege atrazine as a causative agent".

HED Response: A careful reading of the review shows that it is not a review of "incidents that allege atrazine as a causative agent". Commenting on the first database, the Incident Data System, HED states, "Typically no conclusions can be drawn implicating the pesticide as a cause of any of the reported health effects." Commenting on the second database, Poison Control Centers, HED states "PCCs provide telephone consultation for individuals and health care providers on suspected [emphasis added] poisonings."
Syngenta's response focuses mostly on these two databases, but unfortunately missed these key caveats and goes on to mis-characterize these two databases and the significance of their findings.

Syngenta comment: "These databases cover all products containing atrazine, including atrazine that was formulated by many manufacturers and that was used alone or in mixture/sequentially with other pesticides"

HED Response: This comment appears to open the possibility that many incidents were not due to atrazine but rather to mixtures involving other pesticides where the actual pesticide responsible for the incident could not be identified. This is not the case. The HED review excludes those products or cases involving mixtures, when they can be identified, for precisely that reason; so that any effects would be associated with atrazine and not a mixture of pesticides.

Syngenta comment: "Overall, the total number of atrazine incidents is very low when

considering the quantity of product that was handled over the years analyzed. If the number of applications of atrazine were factored into the incident analysis, it is clear that the risk of significant incidents involving humans is extremely low."

HED Response: HED believes the available data support this concluding remark. Normally, an HED review would include a calculation of risk based on the number of incidents occurring in a given time period divided by a surrogate for the population at risk. This provides an incident rate, the primary measure of risk used in epidemiology. Usually the only data source permitting such calculations comes from California where they report on the number of applications, pounds applied, and acreage treated for each active ingredient. California required reporting of all applications by commercial applicators and all applications of restricted pesticides from 1982 through 1989 and since 1990 these data has been collected for all pesticides used in agriculture. Therefore, the comparisons have been limited to that sector of use.

However, atrazine is not widely used in California agriculture and is not even mentioned in their report "An Analysis of Pesticide Use in California, 1991-1995" by Larry Wilhoit et al. (California EPA, Sacramento, California December 1998). Nevertheless, examining the "Pesticide Use Report, Annual 1990 [through 1996], Indexed by Chemical" (California EPA, Sacramento California 1991-97) finds an average of 450 applications per year involving agricultural sites. Normally HED would not calculate ratios of poisoning per thousand applications when the number reported per year is less than 500 because "Ratios were not shown if fewer than 500 applications were reported each year because such ratios would likely be unstable due to small sample size." ("Review of Poison Control Center Data Call In" Memorandum from Jerome Blondell to Joshua First, Dec. 5, 1994).

Assuming there were approximately 500 applications of atrazine over the 15 year period 1982 through 1996 and given only a single reported poisoning where atrazine was deemed the primary pesticide responsible, the ratio would be 0.13 poisonings per 1,000 applications. This compares favorably with the average for selected insecticides which had a median value of 0.41 poisonings per 1,000 applications (Blondell 1994 reference cited above). However, the single case of poisoning was poorly documented and considered a probable case, occurring in 1982. This combined with the relatively small use of atrazine in California prevented calculating a ratio that was judged to be statistically unreliable. Nevertheless, the very low ratio for atrazine suggests that Syngenta's comment that significant incidents are "extremely low" is warranted.

<u>OPP Incident Data System (IDS)</u>

General statement of HED's response to this section:
As noted earlier, Syngenta's extensive comments on this section ignore HED's caveat "Typically no conclusions can be drawn implicating the pesticide as a cause of any of the reported health effects". Further at the beginning of this section HED advised "Please note that the following cases from the IDS do not have documentation confirming exposure or health effects unless otherwise noted". A careful reading of the IDS section does not find evidence documenting exposure or health effects. Therefore, the general HED conclusion from this section was "From

the review of the Incident Data System, it appears that a majority of cases involved skin illnesses such as dermal irritation and pain, rashes, and welts and eye illnesses such as eye damage, blurred vision, conjunctivitis, irritation, and pain." Note this conclusion is entirely consistent with the fifth edition of "Recognition and Management of Pesticide Poisonings" (by J.R. Reigart and J.R. Roberts, USEPA 1999) which states that triazines have the following known or suspected effects: "moderately irritating to the eyes, skin, and respiratory tract".

Syngenta's comment: "The mild symptoms described in this report are consistent with an overexposure to concentrated but not diluted forms of atrazine or products containing atrazine."

HED response: HED agrees that the symptoms consistently reported in the IDS were primarily dermal or ocular and that they may be characterized as mild. However, there is no evidence to say that all of these exposures were due to concentrated product and not diluted product. Animal studies do not fully take into account human variation and should not be extrapolated to assume that some humans might not be sensitive to the effects of diluted atrazine prepared for application.

Syngenta comment: "The few incidents alleging more severe symptoms are not consistent with exposure to concentrated or diluted forms of atrazine or products containing atrazine."

HED response: As noted above, HED did not mention the more severe symptoms in its conclusion. This was because of the lack of documentation of exposure or health effects. Therefore, HED has no serious disagreement with Syngenta's comment in this instance. Syngenta's subsequent comments (pages 320-321) do not add to the basic criticisms already covered and do not change the conclusion of the HED review.

Syngenta comment: "atrazine and products containing atrazine are diluted with water before use which will further decrease the risk of dermal and eye irritation . . . With dilution, all Syngenta products containing atrazine would likely be classified as practically non-irritating to skin and eyes."

HED response: Syngenta's own table listing four atrazine products shows that it can be slightly to mildly irritating to skin and eyes and, in two instances, may be a sensitizer. This supports HED's conclusion from the IDS data that atrazine may cause skin or eye problems which is supported by Reigart and Roberts (1999) statement that atrazine may be irritating to skin, eyes and respiratory tract.

Syngenta comment: Syngenta explicitly denies reports of more severe effects due to lack of documentation and their being contrary to the "atrazine toxicological and epidemiological database".

HED response: As stated before, no conclusion were drawn concerning the more severe effects for the reasons already given by Syngenta and HED.

Poison Control Centers (PCC)

Syngenta comment: "it is likely the majority of incidents contained in the Poison Control Centers data involved minor skin and/or eye irritation".

HED response: The review clearly states "Dermal and ocular effects accounted for the majority of symptoms associated with exposure to atrazine". There is no disagreement here.

Syngenta comment: Syngenta goes on to question whether any of the cases with moderate or more severe symptoms could be attributable to atrazine.

HED response: HED's review clearly states "Note that the excess reported for major effects is based on a single case that reportedly had cardiac arrest and coma. It is not clear from the information on this case why the symptoms were so severe. Examination of cases reporting moderate effects did not show any consistent pattern of reported signs or symptoms and no cases similar to the one major case. This suggests that at least some of the cases had coincidental or unrelated effects to their exposure." There is no disagreement with Syngenta's comment.

Syngenta comment: "Overall, the Agency's presentation of the PCC data does not afford the opportunity for critical analysis, and any conclusions based on this data should be scrutinized or judged as unsupported. The methods for the tabulated values in the PCC data should have been clarified by identifying the rationale and calculations utilized to establish the percentages of outcomes."

HED response: Syngenta's conclusion in these two sentences is not supportable. Their own criticisms show that the data do indeed "afford the opportunity for critical analysis" and the methods used to tabulated an calculate the percentages are clearly spelled out in the text and in the tables of HED's review.

Data provided by the Poison Control Center's is provided only in summary form. Information is usually not available on individual cases and, in any case, is often difficult to obtain due to medical confidentiality concerns. Nevertheless, with a large enough number of cases it is possible to observe patterns that suggest where the risks of exposure to atrazine are likely to occur. Therefore, it is not necessary to analyze each and every case to fully document all aspects of the exposure and document health effects. This attitude that surveillance data lacking documentation is of no value reflects a lack of understanding of the strengths of such information. Syngenta has purposely pointed out only the weaknesses in a biased matter to discredit any information that might reveal a pattern. The Poison Control Center data by itself might be questioned but it is strengthened by other databases and scientific literature.

Other sources of Incident Data

Syngenta comment: Syngenta did not disagree with the finding concerning data from the

California Department of Pesticide Regulation, the National Pesticide Telecommunications Network, or the absence of scientific literature concerning acute poisoning from atrazine. Syngenta goes on to note that more recent data submitted by them in 1998-2000 found the majority of cases were minor. The few cases reporting more serious effects were not supported by exposure data or other documentation that would suggest that atrazine was responsible for the ill effects reported.

HED response: HED has no disagreement with this appraisal.

Syngenta conclusion

Syngenta comment: "Overall, the total number of atrazine incidents is very low especially considering the quantity of product that was handled . . . If the number of applications of atrazine were factored into the incident analysis, it is clear that the risk of significant incidents involving humans is extremely low."

HED response: HED does not disagree with this characterization other than to say that the "risk of significant incidents involving humans appears to be very low" would be a fairer statement given the absence of incidence data with denominators permitting estimating the number of applications in all states but California.

Syngenta comment: With regard to symptoms other than skin and eye irritation, "Based on the information obtained from the extensive atrazine toxicological database and epidemiologic studies, the symptoms claimed in these more significant incidents are due to alternative causes."

HED response: This statement is not warranted because there are no significant epidemiologic studies of exposed field workers. As stated above, toxicological studies cannot always predict human response. A more scientifically justifiable conclusion would have been "the symptoms claimed in these more significant incidents are not supported by sufficient documentation, may be due to alternate causes, and therefore are not a basis for regulatory changes."

Overall Conclusion

The Syngenta review did raise an important point about the very low incident rate of pesticide poisoning due to atrazine. The Health Effects Division agrees that the number of atrazine poisoning appears to be very low and that the overwhelming majority of cases result in minor effects to skin, eyes and respiratory tract. However, the Health Effects Division disagrees with other criticisms concerning the validity of the data and its interpretation.

Response to Attachment 10, "Syngenta/Community Water System Ground Water

Monitoring Study for Atrazine and Its Major Degradation Products in Multiple States in the United States

See response to Attachment 6.

Response to Attachment 11, Atrazine: Chronic Dietary Exosure Assessment for Atrazine and the Simazine Metabolites Common to Atrazine.

Syngenta has submitted a dietary exposure analysis for the uses of atrazine and simazine on corn and sorghum. Once a determination has been made as to which triazines share a common mechanism of toxicity, HED may begin its cumulative exposure assessment for triazine compounds and their metabolites that share a common mechanism of toxicity. HED acknowledges receipt of the attachment and the exposure analysis contained therein, and will review as appropriate.

Response to Attachment 12, Probabilistic Assessment of Drinking Water and Dietary Exposure Combined.

The following is an excerpt from the review memorandum containing HED's review, analysis, and conclusions regarding the submitted probabilistic exposure assessment for chlorotriazines in drinking water and the diet. The entire review can be found in DP Barcode: 278468, C. Eiden, , April 16, 2002.

Previously, HED determined that intermediate-term exposure to chlorotriazines in drinking water occurring during late Spring and early Summer was the only exposure pathway and scenario of concern. All other drinking water and food exposure scenarios analyzed using a deterministic approach resulted in risk estimates that were below HED's levels of concern. HED's Revised Preliminary Human Health Risk Assessment for atrazine (dated 1/19/2001) identified 24 CWS using surface water with seasonal chlorotriazine residues exceeding levels of concern for infants and children. These 24 CWS were identified using a deterministic approach. Consequently, HED concluded that refined estimates of risk for these 24 CWS should be estimated using all of the available data in a probabilistic assessment.

In response to HED's revised preliminary risk assessment, the registrant (Syngenta) has provided a probabilistic exposure assessment for aggregate exposures to chlorotriazine residues in food and the drinking water of 28 CWS. Of these 28 CWS, 24 were identified in the HED risk assessment document as having seasonal concentrations of chlorotriazine residues in drinking water above HED's levels of concern for infants and children.

In addition, the registrant also provided a comparison of the results of probabilistic exposure assessments using two different aggregate exposure models, DISTGEN™ and CALANDEX™. Exposures to chlorotriazine residues in food and drinking water in 5 of the 28 CWS were assessed with each model using the same and different methodologies. A comparison of the results was provided.

Although Syngenta conducted probabilistic assessments for 1-day, short-term, intermediate-term, and chronic exposures, HED has focused only on the results of the submitted intermediate-term probabilistic exposure assessment. Risk estimates associated with intermediate-term exposure to chlorotriazine residues in food and drinking water are presented as a percentage of a population adjusted dose (PAD). Risk estimates greater than 100% of the PAD exceed HED's level of concern. To estimate the risk associated with the 28 CWS assessed, HED has taken the results of the intermediate-term probabilistic exposure assessment conducted by Syngenta, and compared the resultant distribution of exposures to the PAD for intermediate-term effects.

The PAD for intermediate-term effects of chlorotriazine residues is 0.0018 mg/kg/day, and was selected by HED's Hazard Identification Assessment Review Committee (HIARC 12/20/00). It is based on attenuation of the pre-ovulatory luteinizing hormone (LH) surge in rats considered to be a biomarker indicative of atrazine's ability to alter hypothalmic-pituitary function in general. Alteration of the hypothalamic-pituitary function as evidenced through the attenuation of the LH surge was dose-dependent and observed between 1 to 5 months of daily dosing in a 6 month study, making this endpoint an appropriate endpoint to assess intermediate-term (30 days to several months) and chronic (several months to lifetime) exposures to atrazine. Although this specific effect (attenuation of the LH surge) is operative in females, it was selected as the basis for chronic risk assessment for all population subgroups, because it is the most sensitive endpoint available from the toxicity database and therefore protective of other adverse effects, and it is indicative of alterations of the hypothalamic/pituitary/gonadal axis, which may occur in the offspring and adults of other species (humans).

CONCLUSIONS

1. At the 99.9th percentile of exposure, risk estimates for peak seasonal exposures of infants to chlorotriazine residues in drinking water exceed HED's level of concern, i.e., are greater than 100% of the PAD for intermediate-term and chronic effects, in 26 of the 28 CWS analyzed. Of these 26 CWS, 22 serve approximately 128,000 people. (The Shipman reservoir has been excluded as it is no longer serving as a source of drinking water). The population served by the remaining 3 CWS was unavailable. See Table 1.

2. At the 99th percentile of exposure, risk estimates for peak seasonal exposures of infants to chlorotriazine residues in drinking water exceed HED's level of concern in12 of the 28 CWS analyzed. Of these 12 CWS, 8 serve approximately 34,000 people. (The Shipman reservoir has been excluded as it is no longer serving as a source of drinking water). The population served by the remaining 3 CWS was unavailable. Risk estimates for 4 CWS equal 100% of the PAD for intermediate-term effects . See Table 2.

3. At the 95th percentile of exposure, risk estimates for peak seasonal exposures of infants to chlorotriazine residues in drinking water exceed HED's level of concern in 2 of the 28 CWS analyzed. Of these 2 CWS, 1 serves approximately 250 people, the other (Shipman reservoir) has been excluded as it is no longer serving as a source of drinking water. See Table 3.

[Note: The U.S. Census Bureau (2000) estimates that children under 1 year old represent 1.4% of the U.S. population.]

4. Risk estimates for children are less than 100% of the PAD (below HED's level of concern) for intermediate-term effects for all CWS analyzed at the 99th percentile of exposure. Risk estimates for adults are less than 100% of the PAD for intermediate-term effects for all CWS analyzed at the 99.9th percentile of exposure.

5. For the CWS assessed, the dominant exposure pathway for chlorotriazine residues is drinking water. Food exposures to chlorotriazines are insignificant (< 1% of the PAD for intermediate-term effects).

6. Exposure estimates are provided for specific age groups, but not for specific sexes. Exposures for male and female adults are combined.

7. A comparison of different models used to assess exposure to chlorotriazines in drinking water probabilistically indicated that if the same data sets are used and the same methodologies applied to the data, either model provides a similar distribution of exposures. However, if the same data sets are used but different methodologies are applied to the data, the resulting exposures will be different. The methodology used by Syngenta did not incorporate as much variability and randomness as the method preferred by OPP, and likely resulted in less refined estimates of exposure to chlorotriazines in drinking water.

Probabilistic exposure assessments for five of the 28 CWS were conducted using a methodology developed by Novigen, Inc. in consultation with OPP. The results of this assessment were compared to the results from Syngenta's assessment. Two of the 5 CWS assessed using the Novigen methodology resulted in risk estimates at the 99.9th percentile of exposure below HED's level of concern, while three had risk estimates above HED's level of concern. Using the Syngenta methodology, risk estimates for 4 of these 5 CWS were above HED's level of concern, and one was below.

RECOMMENDATIONS

The methodology used by Syngenta to assess exposure to chlorotriazine residues in drinking water probabilistically results in more refined estimates of exposure and risk for the 28 CWS assessed. However, depending on which percentile of exposure is selected as the basis of the risk estimate, the improvement in the risk estimates is limited to only a few CWS. The registrant may want to reconsider the methodology used in the submitted assessment. HED recommends the assessment for the 28 CWS be conducted using the methodology currently approved/used by OPP for cumulative dietary exposure assessment. This is the preferred approach. Specifically, the exposure assessment should include: 1) rolling 90-day exposure periods across the entire 1993 to 2000 data set of chlorotriazine concentrations in finished drinking water for each CWS, 2) separate assessments for male and female adults, and 3) more recent consumption data from the USDA's Continuing Survey of Food Intake by Individuals (CSFII 1994 to 1996). The

preferred methodology should allow sequential daily chlorotriazine concentration values for rolling 90-day periods to be randomly matched with daily consumption values that also vary daily over the rolling 90-day periods for an individual as per CSFII records. This approach to the assessment maximizes randomness and variability, and should result in the most refined estimates of exposure using the available data.

DETAILED CONSIDERATIONS

The general approach to the registrant's submitted probabilistic exposure assessments for 28 CWS are detailed in this section. A separate probabilistic exposure assessment was conducted for each of the 28 CWS. The 24 CWS identified as high risk through HED's revised preliminary risk assessment (1/19/01) are included. Syngenta subsequently identified 4 additional CWS to assess.

Population Subgroups Considered:

The submitted probabilistic exposure assessment considered infants (< 1 year old), children 1 to 6, children 7 to 12, adults 13 to 50 (males and females), and the general population. The specific population distribution for each CWS was based on the US Census (1990) for the specific county served by a given CWS. Each population distribution was weighted as to the number of individuals in a given age and sex group as defined by the census. For example, for the CWS serving Marion Co, IL, the 1990 census data indicated 47.5% females and 52.5% males in the county. Based on percentages, the number of individuals in the county per 1 year age group were then estimated, i.e., males and females < 1 year old, < 2 years old, < 3 years old, etc. In the assessment, drinking water consumption rates and dietary (food) consumption patterns were not linked for an individual, and the assessment for adult males and females is combined.

Exposure Scenarios Considered/Risk Assessments Conducted:

Exposures to chlorotriazine residues in food and drinking water in the identified 28 CWS were assessed for several exposure scenarios: acute (1-day) exposures, short-term (30-day/monthly exposures), intermediate-term (90-day/quarterly exposures), and chronic (multi-year) exposures. The intermediate-term exposure scenario included 2 exposure periods, one period covering exposures during April to June, and a second period covering exposures during May to July.

Toxicological Endpoints Selected:

Syngenta included risk estimates for each population subgroup and exposure scenario. Syngenta selected the following no observed adverse effects levels (NOAELs) and an uncertainty factor of 1000 as the basis of their risk estimates for chlorotriazine residues in food and drinking water:

Table 1. Toxic Endpoints selected for Risk Assessments for Dietary Exposures to Chlorotriazines (Food + Water) by Syngenta Compared to HED's Endpoints				
Exposure Scenario/Endpoints	Acute (1-day)	Short-term (1 to 30 days)	**Intermediate-term (30 days to 6 months)**	Chronic (annual/long-term)
Syngenta's NOAEL (mg/kg/day)	10 (delayed ossification in fetuses & decreased body weight gain in adults)	13 (infants), 6.3 (children), 5.0 (adults)	**13 (prostatitis effects in infants), 6.3 (preputial separation effects for children), 5.0 (attenuation of LH surge in adults)**	1.8 (attenuation of pre-ovulatory LH* surge)
HED's NOAEL (mg/kg/day)	10 (delayed ossification in fetuses & decreased body weight gain in adults)	N/A**	**1.8 (attenuation of pre-ovulatory LH* surge)**	1.8 (attenuation of pre-ovulatory LH* surge)

* Luteinizing hormone. ** HED did not conduct a risk assessment exclusively specific to short-term dietary exposures

HED notes that Syngenta's selection of endpoints and NOAELs for intermediate-term exposures differs from that selected by the HED's Hazard Identification Assessment Review Committee (HIARC). Specifially, Syngenta selected a NOAEL of 13 mg/kg/day for prostatitis effects in the male Wistar rat (offspring) after the mothers were dosed 1 to 4 days post-natally as the basis of short-, and intermediate-term risk assessments on infants. HED considers this a short-term effect (relevant to effects seen within 1 to 30 days of dosing) as it is believed to occur after 1 to 4 days of post-natal maternal dosing. HED does not consider this an intermediate-term effect as used by the registrant in their probabilistic risk assessment. HED selected a NOAEL of 10 mg/kg/day based on the weight-of-evidence from 4 studies investigating developmental effects as the basis of risk assessments on infants and children for short-term exposures.

Syngenta selected a NOAEL of 6.3 mg/kg/day for short-, and intermediate-term risk assessments involving children. HED considers this a short-term effect (relevant to effects seen within 1 to 30 days of dosing) as it is believed to occur after 1 to 4 days of post-natal maternal dosing. HED does not consider this an intermediate-term effect as used by the registrant in their probabilistic risk assessment.

Finally Syngenta selected a NOAEL of 5.0 mg/kg/day as the basis of short-, and intermediate-term risk assessments on adults. This is from a study in which dosing occurred over 30 days. HED does not consider this an intermediate-term effect as used by the registrant in their probabilistic risk assessment. HED selected a NOAEL of 1.8 mg/kg/day for use in intermediate-term risk assessments. This endpoint is from a 6-month subchronic study in which the LH surge was depressed after 4 to 5 months of dosing. Depression of the LH surge is dose and time dependent. HED selected this endpoint for use in intermediate-term (30 days to 6 months) and chronic (6 months to lifetime). This six-month study is considered adequate for use in selecting a chronic endpoint without an additional safety factor being added to account for study duration of less than 12 months. A LH surge study of longer duration may be of limited value given that the attenuation of LH surge occurs in normally aging Sprague-Dawley rats around 9 months of age. Though this endpoint (LH surge attenuation and estrous cycle disruption) is applicable only

to females 13-50, HED's HIARC noted that this dose is the lowest NOAEL available in the toxicology database (i.e., the most sensitive endpoint), and therefore would be protective of other adverse effects, including those occurring in males, infants and children. Further, the attenuation of the LH surge is considered a biomarker indicative of atrazine's ability to alter hypothalamic-pituitary function in general. Therefore, a separate endpoint was not selected for other populations (i.e., males, infants and children).

Syngenta's selection of an uncertainty factor of 1000 is in agreement with that selected by HED's HIARC and Food Quality Protection Act Committee.

Drinking Water Exposures:

The probabilistic exposure assessments included estimates of average daily chlorotriazine concentration for the acute risk assessment, estimates of the monthly average daily concentration for the short-term risk assessment, estimates of the quarterly average daily concentration for the intermediate-term risk assessment, and an estimate of the multi-year average concentration for the chronic risk assessment.

Table 2. Exposure Scenarios Considered	
Exposure Scenario	Chlorotriazine Concentration in Finished Drinking Water
Acute (1-day)	Daily average concentration
Short-term (30 days)	Monthly average daily concentration
Intermediate-term (90 days April to July)	**Quarterly average daily concentration**
Intermediate-term (90 days May to August)	**Quarterly average daily concentration**
Chronic (lifetime)	Multi-year average concentration

For each of the 28 CWS identified, chlorotriazine residues in finished drinking water specific to that CWS were compiled from three data sets: the Voluntary Monitoring Program sponsored by the registrant, data collected under the Safe Drinking Water Act (SDWA), and the Acetochlor Registration Partnership (ARP). Data from these three data sets were pooled for each of the 28 CWS. Under each of these monitoring programs, samples of finished drinking water were taken and anlayzed for atrazine, *per se.* Concentrations of the chlorotriazine metabolites for each CWS were estimated as discussed previously in Attachment VII to HED's revised preliminary risk assessment. Samples of finished drinking water were collected across these monitoring programs during the period from 1993 to 2000.

Data collected from 1993 to 2000 were organized by exposure period, i.e., consecutive 30-day (monthly) periods, or 90-day (quarterly) periods, and average concentrations for the time period were determined. For example, for the intermediate-term exposure assessments, data were organized by quarters (Jan/Mar, Apr/Jun, Jul/Sep, and Oct/Dec), and the 90-day (quarterly) average concentration (ug/kg/day) for each quarter was determined. This resulted in a

distribution of approximately 28 point estimates of quarterly average chlorotriazine concentrations from 1993 to 2000 (4 quarterly averages per year x 7 years) used in the assessment.

Drinking water consumption rates (ml/kg/day) included in the registrant's exposure assessments were based on data collected under the USDA's Continuing Survey of Food Intake by Individuals (CSFII). The consumption rates used for adults are based on data from the CSFII 1977-1978, and broken down into the following age subgroups: adults 20 to 44, 45 to 64, 65 to 74, and 75 + years old. The consumption rates used for children are based on the CSFII data from 1989-1992, and broken down into the following age subgroups: infants (< 1 year old), children (1- 10 years old), and adolescents (11 to 19 years old). Consumption rates for adults were taken from Table 3-7 of the USEPA's "Exposure Factors Handbook, Volume I" (August 1997), and consumption rates for infants and children were taken from Table 4-2 from the USEPA's "Estimated Per Capita Water Ingestion in the U.S." (April 2000). Consumption rates were combined for males and females for each age group assessed. This resulted in a distribution of drinking water consumption rates which included the 1st, 5th, 10th, 25th, 50th, 75th, 90th, 95th, and 99th consumption percentiles for each of these age groups (given below in table 3). It is not clear if only this portion of the consumption distribution for water was used or the entire distribution.

Table 3. Drinking Water Consumption Rates

Age (years)	Percentiles of Water Intake (ml/kg/day)								
	1%	5%	10%	25%	50%	75%	90%	95%	99%
<1	0	0	0	16	57	101	156	170	218
1 - 10	0	4	6	12	21	33	49	64	98
11 - 19	0	2	4	7	13	20	30	39	64
20 - 44	1.6	4.9	7.1	11.2	16.8	23.7	32.2	38.4	53.4
45 - 64	4.4	8.0	10.3	14.7	20.2	27.2	35.5	42.1	57.8
65 -74	4.6	8.7	10.9	15.1	20.2	27.2	35.2	40.6	51.6
75+	3.8	8.8	10.7	15.0	20.5	27.1	33.9	38.6	47.2

Food Exposure:

The assessment included average daily dietary exposure (mg/kg/day) to the chlorotriazines through food as a point estimate. That is, the assessments assume that an individual within a specific age/sex population subgroup receives the same daily (constant) exposure to chlorotriazines in food during the exposure period assessed. Point estimates of dietary exposure were taken from HED's chronic dietary assessment as given in Attachment V to HED's revised preliminary risk assessment. HED's dietary assessment included anticipated residue concentrations of chlorotriazines in foods combined with average dietary consumption of food and average body weights collected under the CSFII 1989-1992. The results of that chronic

dietary assessment for exposure to chlorotriazines in foods are given below in table 4:

Table 4. Chronic Dietary Exposure	
Population Subgroup	Average Daily Dietary Exposure (mg/kg/day)
Infants (< 1 year old)	0.000008
Children 1 to 6	0.000017
Children 7 to 12	0.000009
Females 13 to 50	0.000003
Males 13 to 19	0.000006
Males 19 to 50	0.000003
Seniors	0.000003

These point estimates of dietary exposure to the chlorotriazines represent an average, constant daily exposure, and not a 99.9th percentile dietary exposure as stated in the registrant's submitted report.

For the acute (1- day) exposure assessment, this approach combines a distribution of daily average chlorotriazine concentrations in drinking water with a point estimate of average daily chlorotriazine exposures in foods. For all other drinking water exposures considered, this approach combines a distribution of average monthly, quarterly, or lifetime exposure with a point estimate of average daily chlorotriazine exposures in foods. The registrant included a point estimate of 4.5×10^{-6} mg/kg/day for the average food exposures for adults, which is the average of the combined female food exposure with the average food exposure for the most highly exposed male population subgroup.

Combining Intermediate-term Drinking Water and Food Exposures Probabilistically:

In the intermediate-term drinking water exposure assessment, drinking water consumption rates and dietary (food) consumption patterns were not linked for an individual. The registrant's assessment assumes the same daily drinking water consumption rate (a point estimate taken from a distribution of consumption rates as described in the table 3) for an individual (within a given age group) throughout the entire exposure period assessed. Consequently, a specific individual's drinking water consumption rate does not vary (is fixed) during the exposure assessment. For example, for the intermediate-term exposure assessments, if the consumption rate randomly selected for an individual from the distribution of rates is 16.8 ml/kg/day, representing the 50^{th} percentile consumption rate for adult males and females ages 20 to 44, that consumption rate is assumed for that individual everyday during the 90-day exposure period.

Chlorotriazine concentrations (ug/kg/day) in drinking water are included in the intermediate-term assessment as a randomly selected quarterly average (a point estimate) from a distribution of

quarterly averages. The same daily quarterly (90-day) average chlorotriazine concentration is assumed to occur in the drinking water consumed by an individual throughout the entire 90–day exposure period.

An individual's drinking water exposure to chlorotriazine is estimated by multiplying the randomly selected drinking water consumption (ml/kg/day), which is fixed during the 90-day exposure period, by the randomly selected 90-day average chlorotriazine concentration (ug/kg/day), which is also fixed during the 90-day exposure period. Conversion factors are applied to obtain the results in mg/kg/day. Food exposure (mg/kg/day) is then added as a point estimate representing average food exposures for a specific age group from table 4 to the estimated drinking water exposure. Consumption rates and food exposures are specific to age population subgroups, as previously described, but not specific as to sex. The resulting distribution of exposures represents the average quarterly (90-day) exposure to chlorotriazines in food and drinking water for individuals representing the population at each CWS by specific population subgroups defined by age.

Results (Risk Estimates) for Intermediate-Term (Seasonal) Drinking Water and Food Exposure:

The results for the probabilistic assessment of intermediate-term (seasonal) exposures to the chlorotriazines in food and drinking water are discussed in this section. Although informative, probabilistic assessments of exposure for other exposure periods were not considered necessary and are not discussed in this memorandum, because risk estimates for these other durations of exposure assessed under HED's revised preliminary assessment did not exceed HED's level of concern.

To estimate risk, the distribution of dietary exposures to chlorotriazines are compared to a toxic reference dose or population adjusted does (PAD) for intermediate-term effects. HED has selected 0.0018 mg/kg/day as the relevant toxic reference dose for chlorotriazine residues for comparison to intermediate-term dietary exposures (30 days to 6 months) to chlorotriazines. The 95^{th}, 99^{th}, and 99.9^{th} percentiles of exposure for infants, children (1 to 6 years old) and adults (male and female combined) were taken from Syngenta's probabilistic exposure assessment for each of the 28 CWS and compared to this PAD.

At the 99.9^{th} percentile of exposure, risk estimates for peak seasonal exposures of infants to chlorotriazine residues in drinking water exceed HED's level of concern, i.e., are greater than 100% of the PAD for intermediate-term effects, in 26 of the 28 CWS analyzed. Of these 26 CWS, 22 serve approximately 128,000 people. (The Shipman reservoir has been excluded as it is no longer serving as a source of drinking water). The population served by the remaining 3 CWS was unavailable. See Table 1.

At the 99^{th} percentile of exposure, risk estimates for peak seasonal exposures of infants to chlorotriazine residues in drinking water exceed HED's level of concern in12 of the 28 CWS analyzed. Of these 12 CWS, 8 serve approximately 34,000 people. (The Shipman reservoir has been excluded as it is no longer serving as a source of drinking water). The population served by

the remaining 3 CWS was unavailable. Risk estimates for 4 CWS equal 100% of the PAD for intermediate-term effects . See Table 2.

At the 95th percentile of exposure, risk estimates for peak seasonal exposures of infants to chlorotriazine residues in drinking water exceed HED's level of concern in 2 of the 28 CWS analyzed. Of these 2 CWS, 1 serves approximately 250 people, the other (Shipman reservoir) has been excluded as it is no longer serving as a source of drinking water. See Table 3.

[Note: The U.S. Census Bureau (1990) estimates that children under 1 year old represent 1.4% of the U.S. population.]

Risk estimates for children are less than 100% of the PAD (below HED's level of concern) for intermediate-term effects for all CWS analyzed at the 99th percentile of exposure. Risk estimates for adults are less than 100% of the PAD for intermediate-term effects for all CWS analyzed at the 99.9th percentile of exposure.

For the CWS assessed, the dominant exposure pathway for chlorotriazine residues is drinking water. Food exposures to chlorotriazines are insignificant (< 1% of the PAD for intermediate-term effects).

Exposure estimates are provided for specific age groups, but not for specific sexes. Exposures for male and female adults are combined.

Appendices I- III contain the exposure and risk estimates for seasonal exposures to chlorotriazines in food and drinking water.

Comparison of Methodologies Used to Probabilistically Assess Exposure:

Probabilistic exposure assessments for five of the 28 CWS were conducted using a methodology developed by Novigen, Inc. in consultation with OPP. The results of this assessment were compared to the results from Syngenta's assessment discussed above. Two of the 5 CWS assessed using the Novigen methodology resulted in risk estimates at the 99.9th percentile of exposure below 100% of the PAD, i.e., below HED's level of concern, while three had risk estimates greater than 100% of the PAD, i.e., above HED's level of concern. Using the Syngenta methodology, risk estimates for 4 of these 5 CWS were above HED's level of concern, and one was below. The differences in the methodologies are discussed below.

The Novigen methodology included the full distribution of drinking water consumption rates (ml/kg/day) as reported for each individual included in the 1994 to 1996 CSFII. In the Novigen approach, a daily consumption rate is randomly selected from this distribution for an individual. Therefore, an individual's water consumption rate varies from day to day within the exposure period of interest versus the fixed consumption rate used in the Syngenta assessment, which is constant during the exposure period of interest.

For each of the 5 CWS assessed, Novigen determined the specific period during which the maximum daily chlorotriazine concentrations occurred for each year of data, selected the year with the highest period of daily concentrations, and then used this as a truncated distribution representing the peak period of chlorotriazine concentrations for that CWS in the 7-year period for which data were available. This resulted in a truncated distribution consisting of daily concentration values covering a variable time period (spanning weeks to months) for a specific CWS. For example, one CWS had a peak period of concentrations spanning a 12 month period. For this CWS, the daily concentrations covering those 12 months were used as a truncated distribution. Another CWS had a peak period of concentrations spanning 2 months. For this CWS, the daily concentrations covering those 2 months were used as a truncated distribution. The Novigen assessment included chlorotriazine concentration data from raw and finished drinking water where available for a given CWS.

In Novigen's assessment, daily concentration values from these distributions representing the highest exposures for each CWS were randomly selected and combined with the randomly selected individual consumption rates from the CSFII. The average 90-day exposure is then calculated from the daily estimates of exposure over the 90-day period. The average food exposure is added in as a point estimate to the 90-day average drinking water exposures as per Syngenta's assessment. In Novigen's assessment an individual's water consumption rate and daily concentration value of chlorotriazines varies from day to day within the exposure period of interest versus the fixed consumption rate and fixed average concentration assumed during the exposure period of interest used in the Syngenta assessment. The resulting distributions of exposure from Novigen's assessment show more variability than the distributions of exposure obtained form Syngenta's assessment. The lower percentiles of the resulting distributions of exposure are lower than those generated by Syngenta, while the upper percentiles are higher.

Raw Water versus Finished Water:

Syngenta included a probabilistic exposure assessment for the 20 CWS for which chlorotriazine concentration data were available in raw and finished drinking water. For each of these 20 CWS, all monitoring data on both raw (untreated) and finished (treated) water were combined. The results of this assessment indicate that combining daily concentration values on atrazine residues in raw and finished water had almost no effect on the resulting exposure assessment. Under this approach, 27 out of 28 CWS had atrazine levels exceeding HED's level of concern at the 99.9th percentile of exposure. Using only data on finished drinking water, 26 out of 28 CWS had atrazine residue levels exceeding HED's level of concern. An examination of the data indicate that concentrations of atrazine residues in raw water are similar to those in finished water at the upper end of the distribution. Appendix IV contains estimates of exposures and risks at the 99.9^{th} percentile of exposure for the combined raw and finished water data sets.

APPENDIX I

Risk Estimates @ the 99.9th Percentile of Exposure for Seasonal Exposures to Atrazine in Food and Finished Drinking Water

Table 1.__ Risk Estimates for High Seasonal Exposures to Atrazine in Finished Drinking Water and Average Dietary Exposure @ the 99.9th Percentile of Exposure*

Community Water System (City/State)	Infant's Exposure (mg/kg/day)	% cPAD	Children's Exposure (mg/kg/day)	% cPAD	Adult's Exposure (mg/kg/day)	% cPAD
Chariton, IA	0.0021	**117**	0.00086	48	0.0005	28
Sorento, IL	0.0019	**105**	0.00087	48	0.00049	27
Flora, IL	0.0021	**116**	0.00089	49	0.00055	30
W. Salem, IL	0.0026	**144**	0.0012	66	0.00063	35
Farina, IL	0.0028	**155**	0.001	55	0.00068	38
White Hall, IL	0.0033	**183**	0.0015	83	0.00078	43
Carlinville, IL	0.0018	**100**	0.00083	46	0.00042	23
Gillespie, IL	0.006	**333**	0.0025	**139**	0.0014	78
Hettick, IL	0.0062	**344**	0.0023	**128**	0.0015	83
Shipman, IL	0.0069	**383**	0.0029	**161**	0.0017	94
Palmyra-Modesto, IL	0.0043	**239**	0.0018	100	0.00096	53
N. Otter Twp ADGPTV, IL	0.0025	**139**	0.001	56	0.00061	34
Kinmundy, IL	0.0025	**139**	0.00094	52	0.00055	31
Salem, IL	0.0072	**400**	0.0031	**172**	0.0017	94
Centralia, IL	0.0024	**133**	0.0011	61	0.00058	32
Hillsboro, IL	0.0034	**189**	0.0013	72	0.00083	46
Wayne City, IL	0.0015	83	0.0006	33	0.00036	20
Louisville, IL	0.0032	**178**	0.0013	72	0.00074	41
Holland, IN	0.0036	**200**	0.0015	83	0.00083	46
North Vernon, IN	0.0027	**150**	0.001	56	0.00067	37

Table 1.__ Risk Estimates for High Seasonal Exposures to Atrazine in Finished Drinking Water and Average Dietary Exposure @ the 99.9th Percentile of Exposure*						
Community Water System (City/State)	Infant's Exposure (mg/kg/day)	% cPAD	Children's Exposure (mg/kg/day)	% cPAD	Adult's Exposure (mg/kg/day)	% cPAD
Batesville, IN	0.0033	**183**	0.0012	67	0.00078	43
Scottsburg, IN	0.0039	**217**	0.0016	89	0.00087	48
Iberville, LA	0.0028	**156**	0.0012	67	0.00061	34
Higginsville, MO	0.0043	**239**	0.0016	89	0.00094	52
Bucklin, MO	0.0029	**161**	0.0012	66.7	0.00072	40
Vandalia, MO	0.0024	**133**	0.001	56	0.00055	31
Sardinia, OH	0.0076	**422**	0.0029	**161**	0.0018	100
Newark, OH	0.0013	72	0.00058	32	0.00033	18

* The exposure estimates include an average (point estimate) dietary exposure of 8×10^{-6} mg/kg/day for infants (< 1 year old), 1.7×10^{-5} for children (1 to 6 years old), and 4.5×10^{-6} for adults (males and females).

APPENDIX II

Risk Estimates @ the 99th Percentile of Exposure for Seasonal Exposures to Atrazine in Food and Finished Drinking Water

Table 2.__ Risk Estimates for High Seasonal Exposures to Atrazine in Finished Drinking Water and Average Dietary Exposure @ the 99th Percentile of Exposure*

Community Water System (City/State)	Infant's Exposure (mg/kg/day)	% cPAD	Children's Exposure (mg/kg/day)	% cPAD	Adult's Exposure (mg/kg/day)	% cPAD
Chariton, IA	0.0013	72	0.00043	24	0.00029	16
Sorento, IL	0.0013	72	0.00049	27	0.00031	17
Flora, IL	0.0016	89	0.00056	31	0.00036	20
W. Salem, IL	0.0016	89	0.00061	34	0.00039	22
Farina, IL	0.0018	100	0.00064	36	0.0004	22
White Hall, IL	**0.0024**	**133**	0.00085	47	0.00053	29
Carlinville, IL	0.0012	67	0.00043	24	0.00027	15
Gillespie, IL	**0.0034**	**189**	0.0011	61	0.00085	47
Hettick, IL	**0.0039**	**217**	0.0015	83	0.00093	52
Shipman, IL	**0.0049**	**272**	0.0016	89	0.0011	61
Palmyra-Modesto, IL	**0.0029**	**161**	0.00099	55	0.0006	33
N. Otter Twp ADGPTV, IL	0.0018	100	0.0006	33	0.00036	20
Kinmundy, IL	0.0015	83	0.00052	29	0.00033	18
Salem, IL	**0.0049**	**272**	0.0016	89	0.00099	55
Centralia, IL	0.0017	94	0.0006	33	0.00038	21
Hillsboro, IL	0.0018	100	0.00063	35	0.0004	22
Wayne City, IL	0.0011	61	0.00037	21	0.00023	13
Louisville, IL	**0.0021**	**117**	0.00078	43	0.0005	28
Holland, IN	**0.0023**	**128**	0.00077	43	0.00048	27
North Vernon, IN	0.0016	89	0.0006	33	0.00039	22
Batesville, IN	**0.002**	**111**	0.00072	40	0.00046	26

Table 2.__ Risk Estimates for High Seasonal Exposures to Atrazine in Finished Drinking Water and Average Dietary Exposure @ the 99th Percentile of Exposure*						
Community Water System (City/State)	Infant's Exposure (mg/kg/day)	% cPAD	Children's Exposure (mg/kg/day)	% cPAD	Adult's Exposure (mg/kg/day)	% cPAD
Scottsburg, IN	**0.0021**	**117**	0.00073	41	0.00048	27
Iberville, LA	0.0018	100	0.00069	38	0.00041	23
Higginsville, MO	**0.0026**	**144**	0.00085	47	0.00057	32
Bucklin, MO	0.0018	100	0.00066	37	0.00042	23
Vandalia, MO	0.0014	78	0.00052	29	0.00032	18
Sardinia, OH	**0.0041**	**228**	0.0013	72	0.0011	61
Newark, OH	0.001	56	0.00034	19	0.00022	12

* The exposure estimates include an average (point estimate) dietary exposure of 8×10^{-6} mg/kg/day for infants (< 1 year old), 1.7×10^{-5} for children (1 to 6 years old), and 4.5×10^{-6} for adults (males and females).

APPENDIX III

Risk Estimates @ the 95th Percentile of Exposure for Seasonal Exposures to Atrazine in Food and Finished Drinking Water

Table 3.___ Risk Estimates for High Seasonal Exposures to Atrazine in Finished Drinking Water and Average Dietary Exposure @ the 95th Percentile of Exposure*

Community Water System (City/State)	Infant's Exposure (mg/kg/day)	% cPAD	Children's Exposure (mg/kg/day)	% cPAD	Adult's Exposure (mg/kg/day)	% cPAD
Chariton, IA	0.0005	28	0.0002	11	0.00014	8
Sorento, IL	0.00078	43	0.00028	16	0.00019	11
Flora, IL	0.00076	42	0.00029	16	0.0002	11
W. Salem, IL	0.00093	52	0.00034	19	0.00022	12
Farina, IL	0.00098	54	0.00037	21	0.00023	13
White Hall, IL	0.0012	67	0.00043	24	0.0003	17
Carlinville, IL	0.00065	36	0.00023	13	0.00015	8
Gillespie, IL	0.00092	51	0.00037	21	0.00026	14
Hettick, IL	**0.0022**	**122**	0.00077	43	0.00052	29
Shipman, IL	**0.0021**	**117**	0.00076	42	0.00053	29
Palmyra-Modesto, IL	0.0014	78	0.0005	28	0.00034	19
N. Otter Twp ADGPTV, IL	0.0009	50	0.00033	18	0.00021	12
Kinmundy, IL	0.00069	38	0.00026	14	0.00017	9
Salem, IL	0.0013	72	0.00054	30	0.0004	22
Centralia, IL	0.00088	49	0.00033	18	0.00022	12
Hillsboro, IL	0.0007	39	0.00027	15	0.00018	10
Wayne City, IL	0.00045	25	0.00018	10	0.00012	7
Louisville, IL	0.0012	67	0.00042	23	0.00029	16
Holland, IN	0.00093	52	0.00034	19	0.00024	13
North Vernon, IN	0.00077	43	0.00029	16	0.00019	11

Table 3.___ Risk Estimates for High Seasonal Exposures to Atrazine in Finished Drinking Water and Average Dietary Exposure @ the 95th Percentile of Exposure*						
Community Water System (City/State)	Infant's Exposure (mg/kg/day)	% cPAD	Children's Exposure (mg/kg/day)	% cPAD	Adult's Exposure (mg/kg/day)	% cPAD
Batesville, IN	0.00094	52	0.00034	19	0.00023	13
Scottsburg, IN	0.00082	46	0.0003	17	0.00022	12
Iberville, LA	0.00091	51	0.00034	19	0.00022	12
Higginsville, MO	0.00076	42	0.0003	17	0.00022	12
Bucklin, MO	0.00058	32	0.00025	14	0.00018	10
Vandalia, MO	0.00073	41	0.00026	14	0.00018	10
Sardinia, OH	0.00068	38	0.00029	16	0.00022	12
Newark, OH	0.00051	28	0.0002	11	0.00012	7

* The exposure estimates include an average (point estimate) dietary exposure of 8×10^{-6} mg/kg/day for infants (< 1 year old), 1.7×10^{-5} for children (1 to 6 years old), and 4.5×10^{-6} for adults (males and females).

APPENDIX IV

Risk Estimates for Seasonal Exposures to Atrazine in Food and Finished and Raw Drinking Water

Table 4.___ Risk Estimates for High Seasonal Exposures to Atrazine in Finished and Raw Drinking Water and Average Dietary Exposure @ the 99.9th Percentile of Exposure*

Community Water System (City/State)	Infant's Exposure (mg/kg/day)	% cPAD	Children's Exposure (mg/kg/day)	% cPAD	Adult's Exposure (mg/kg/day)	% cPAD
Chariton, IA	0.0021	117	0.00086	48	0.0005	28
Sorento, IL	0.0019	105	0.00084	47	0.00049	27
Flora, IL	0.0021	117	0.00089	49	0.00055	30
W. Salem, IL	0.0026	144	0.0012	67	0.00063	35
Farina, IL	0.0028	155	0.001	55	0.00068	38
White Hall, IL	0.0033	183	0.0015	83	0.00078	43
Carlinville, IL	0.0028	155	0.0012	67	0.00066	37
Gillespie, IL	0.006	333	0.0025	139	0.0014	78
Hettick, IL	0.0062	344	0.0023	128	0.0015	83
Shipman, IL	0.0069	383	0.0029	161	0.0017	94
Palmyra-Modesto, IL	0.0043	239	0.0018	100	0.00097	54
N. Otter Twp ADGPTV, IL	0.0026	144	0.0011	61	0.00063	35
Kinmundy, IL	0.0025	139	0.00094	52	0.00055	30
Salem, IL	0.0072	400	0.0031	172	0.0017	94
Centralia, IL	0.0031	172	0.0015	83	0.00075	42
Hillsboro, IL	0.0031	172	0.0013	72	0.00077	43
Wayne City, IL	0.0026	144	0.00099	55	0.00057	32
Louisville, IL	0.0032	178	0.0013	72	0.00074	41
Holland, IN	0.0036	200	0.0015	83	0.00083	46
North Vernon, IN	0.0027	150	0.001	55	0.00067	37
Batesville, IN	0.0033	183	0.0012	67	0.00078	43
Scottsburg, IN	0.0039	217	0.0016	89	0.00087	48

Table 4.___ Risk Estimates for High Seasonal Exposures to Atrazine in Finished and Raw Drinking Water and Average Dietary Exposure @ the 99.9th Percentile of Exposure*						
Community Water System (City/State)	Infant's Exposure (mg/kg/day)	% cPAD	Children's Exposure (mg/kg/day)	% cPAD	Adult's Exposure (mg/kg/day)	% cPAD
Iberville, LA	0.0028	155	0.0012	67	0.00062	34
Higginsville, MO	0.0043	239	0.0016	89	0.00094	52
Bucklin, MO	0.0029	161	0.0012	67	0.00072	40
Vandalia, MO	0.0028	155	0.0012	67	0.00073	40
Sardinia, OH	0.0075	417	0.003	167	0.0018	100
Newark, OH	0.0013	72	0.00058	32	0.00033	18

* The exposure estimates include an average (point estimate) dietary exposure of 8×10^{-6} mg/kg/day for infants (< 1 year old), 1.7×10^{-5} for children (1 to 6 years old), and 4.5×10^{-6} for adults (males and females).